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# THE UNDERSTANDING OF INVOLUNTARY MOVEMENTS: AN HISTORICAL APPROACH[1]

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In man's eternal quest for knowledge, nothing is insignificant. From the atoms to the stars, his search goes on for an understanding of Nature, and, perhaps, of God.

In this adventure, the physician holds a privileged position. From the bedside, he is a witness to human misery and to human hope. He must tend to the former and fortify the other. But to do this properly, he must have knowledge and understanding, faith and wisdom.

The physician's philosophy of Life cannot, and must not, be materialistic if he is to remain true to his oath. Ambroise Paré used to say, "Je le pansai, Dieu le guérit" and despite the formidable advances of modern science, this is still realistic.

But, a philosophy of Life is not built in one day. It comes from the daily contact with human frailty, from the treasures of human relationships and from the teachings of history.

To the student of Medicine, the complexity of disease is such that a purely descriptive and pseudo-scientific approach often becomes the easiest way to Knowledge. One can treat Paralysis Agitans without knowing about James Parkinson, and one could conceivably do research on the functions of the globus pallidus without having heard of Cecile and Oskar Vogt, but one will never understand the true nature of diseases without reading the original descriptions and the most important contributions.

In the light of history the miseries of man become more human, more understandable. The failures of physicians and patients alike do not appear so useless and when the overall picture is considered, signs of progress and improvement are more evident—a ray of hope is more justified.

We propose in this paper to review a few pages of the story of involuntary movements. This, in one way, is the story of man's credulity and ignorance, but it is also the story of one of the most difficult problems confronting neurologists and physiologists. For the most part, it is not the story of great men, but that of astute observers, simple and honest practitioners, devoted to the care of sufferers. Very few of the heroes we will mention knew the rewards of fame during their lives and many contributors, whose names we do not even remember, lie forgotten behind the tombstones of the more famous.

## MIDDLE AGES

The story of involuntary movement does not, as one would expect, go back to the Greeks. Hippocrates makes no mention of this kind of disorder. Occasionally the word Scelotyrben appears in the literature and probably derives from the Greek σχελος: leg and θνρβη: weakness or perturbation, but there is doubt as to its true meaning. Some of the miracles reported in the Bible undoubtedly represent the cure of types of involuntary movements, whether physiological or hysterical in nature. The great Galen, himself, only mentions a form of incomplete

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paralysis of the lower limbs and gives no explanation of abnormal movements.

Strangely enough, our story is born in one of the most ancient expressions of man's religion and joy: dancing. Man dances to celebrate his victories, to exercise his limbs, to demonstrate his love. He used dances to tell stories and to worship his Gods. To the pace of music he can be melodious or lose himself in complete intoxication. Man has expressed his most beautiful sentiments in the form of music and dances but he has also used the stimulation of mass imitation to gather courage for his battles. The Indians of America, like the natives of Africa and Polynesia always dance before a hunt or a raid. Gradually kindled by the shamans or medicine men, the intoxication becomes such that the meeker are driven to frenzy. Auto-intoxication is induced intentionally or incidentally by dancing and certainly the best known examples are the wild excesses of the Bacchanals or the sexual dances of the Polynesians (17). Some dances are known to imitate the gambols of the wolf and bear or other wild beasts. The Ostyak tribes of northern Asia dance in sudden leaps and violent turns, which exhaust the muscular power of the whole body. The Bushmen also dance in long irregular jumps.

But the strangest dances of all are certainly the ones that the world witnessed in the darkest hours of the Middle Ages. The phenomenon of the Dark Ages is a strange one indeed and a sad one at that. One shudders at the memory of the Inquisition and the fight against heresy, and one is almost unable to believe the miseries of the great epidemics that destroyed large portions of the living world (29). Only in a period of total ignorance and blind credulity can such events occur, but the centuries before the Renaissance were ripe for the strangest of maladies.

The first sign of the impending epidemic occurred in the year 1027 in Kolbig, but the worst disaster the world had ever known struck in 1348. The extent of the Plague, known as the Black Death, cannot be understood nowadays, even with the accounts of Hecker and Petrarch. The story in all its horror and ominous memories is told in one of the world's most widely read books, Boccaccio's "Decameron."

The logical explanation of such a calamity could only be found in the belief that man was suffering in expiation of his sins and the Church used the uncontrollable fear of the nations to establish more firmly its control. People were nervous and confused and it is not surprising that at Aix-La-Chapelle, in the year 1374, a strange new disease was born.

In that year, the fear that gripped most of humanity was so great that the occasion of the famous festival of St. John the Baptist soon created wild orgies. "People formed circles hand in hand, and appearing to have lost all control over their senses, continued dancing regardless of the bystanders, for hours together, in wild delirium, until at length they fell to the ground in a state of exhaustion. They then complained of extreme oppression, and groaned as if in the agonies of death, until they were swathed in cloths bound tightly round their waists, upon which they again recovered and remained free from complaint until the next attack." (29) Most of the sufferers had vivid hallucinations, generally of the Saviour or the Virgin Mary and encouraged by the priests who tried to stop them, they formed processions, dancing and jumping and singing, "St. John so, so, brisk and cheerful St. John."

This new and strange epidemic spread rapidly to many countries where it was known under different names. In Germany it was called St. John's or St. Vitus' Dance; in France, "Danse de St. Guy." The Latin name of "Chorea Sancti Viti" is the best known. The disease, obviously mainly hysterical in nature, did not completely disappear for it was still described in the 16th

Century and episodic occurrences were still known in parts of the world till the last century, being variously known as Tarantism, Astaragaza, "Leaping Ague," "convulsionnaires," "Jumpers," "Rollers" and "Barkers."

This dansomania is not a phenomenon limited to the Dark Ages. It is the result of superstition, libertinage, religious exaltation. It is spread through imitation, "sympathy" and imposture. Most of these epidemics received the generic term of chorea from the Greek word meaning dance.

The first man to look more closely into the problem of the choreas was an erratic, unbalanced mystic, who was also a great reformer: Philippus Aureolus Theophrastus Paracelsus Bombastus von Hohenheim (1493–1541), better known as Paracelsus. The character of this man is exceptional. From the day of his inauguration, when he is said to have burned in public all the old textbooks, to the time of his death, he was a non-conformist. He always used the vernacular in contrast to the learned habit of his time, where Latin was the only scientific language. He even wrote, "Since I saw that the doctrine accomplished nothing but the making of corpses, deaths, murder, deformity, cripples and decay, and had no foundation, I was compelled to pursue the truth in another way, to seek another basis, which I have attained after hard labor." (31) Arrogant and bombastic in public, he became humane and charitable in the presence of the sick and was a keen observer of symptoms and signs.

Because of this respect for disease, he was the first to separate chorea imaginata and chorea lascivia from chorea naturalis. The dancing manias of the Middle Ages are classified among the chorea lascivia. Chorea naturalis to him is a milder form, where only anxiety, confusion and involuntary spasmodic laughter are present. He thought this form to be of natural cause and is confirmed in his belief by Shenckius of Graffenberg in 1607 (72).

### THOMAS SYDENHAM AND CHOREA

But the man who is universally recognized as the father of chorea is the "English Hippocrates" Thomas Sydenham (1624–1689), a man who was never even elected to the Fellowship of the Royal College of Physicians, but whose name is remembered along with those of only two important contemporaries: William Harvey and John Locke.

Born in Wynford Eagle, England, he was baptized on September 10, 1624. His family could boast of many important ancestors and it is believed that their financial position was more than satisfactory. He went to school at Magdalen Hall where he matriculated as a Fellow commoner on May 20, 1642. He then went to Oxford, but his studies were soon interrupted by the political events of the time. The Civil War of Britain opposed the forces of the Parliamentary army (in which Thomas and his brothers served) and those of the King. After the war, a chance meeting with Dr. Thomas Coxe led him to the study of medicine. Because the political affiliations of Oxford had now changed and because of the shortage of licensees, a number of degrees were then given "by creation." Through this strange process, Sydenham was created "Bachelor of Medicine" on April 14, 1648, by command of the Earl of Pembroke." At the most, he had served one year as a resident at the University, but again, through political influence, he replaced an expelled Royalist as Fellow of All Soul's College in the same year. Luckily for the medical profession, he soon resigned this commission and started in practice around 1656. He moved to London and settled in Westminster, but only for a short time for it is believed that in 1659, he was at Montpellier studying under the then famous Charles Barbeyrac, whom his friend Locke had rec-

ommended. He was back in London by 1660 and obtained his license to practice from the Royal College in 1663 at 39 years of age (62).

By then, he had become interested in the study of fevers, the most prevalent diseases of his time and soon the city of London was visited by the famous Great Plague of 1664–1665, which killed close to 70,000 people. Unfortunately, and the fact is always deplored by his apologists, he fled the city to retire in the country, as he says "compelled by his friends." During that year he published his first medical work of importance, "The Treatment of Fevers." The method he prescribed caused quite some resentment amongst his contemporaries for he preconized the cooling method, in complete reversal to the accepted technics.

Sydenham was a scrupulous observer and an astute physician. He described in detail the gout, from which he suffered, and hysteria, which he found more common among women. His description of measles, chicken pox, dysentery and scarlet fever are classics. For them he never received distinctions, but he brushed this off with the statement, "I have weighed on a nice scrupulous balance whether it be better to serve men or to be praised by them, and I prefer the former." He had a profound disrespect for the knowledge of his times. One day, Dr. Richard Blackmore asked him what books he should read to gain knowledge of medicine and he answered, "Read Don Quixote. It is a very good book. I read it myself still." (65).

Despite, or because of this, he consigned his own observations in a book that is now famous: *Schedula Monitoria de Novae Febris Ingressa*, published in 1686. The book was dedicated to "the most excellent and learned Charles Goodall, M.D., Fellow of the College of Physicians in London." The main part was called "Processus Integri" and contained the famous descriptions of Hysteria (Ch. 1) and "Chorea Sancti Viti" (Ch. 16).

The description of chorea is short but very concise and is worth citing here:

"St. Vitus Dance is a sort of convulsion which attacks boys and girls from the tenth year until they have done growing. At first it shows itself by a halting, or rather an unsteady movement of one of the legs, which the patient drags. Then it is seen in the hand of the same side. The patient cannot keep it a moment in its place, whether he lay it upon his breast or any part of his body. Do what he may, it will be jerked elsewhere convulsively. If any vessel filled with drink be put into his hand, before it reaches his mouth, he will exhibit a thousand gesticulations like a mountebank. He holds the cup straight, as if to move it to his mouth, but has his hand carried elsewhere by sudden jerks. Then, perhaps, he contrives to bring it to his mouth. If so, he will drink the liquid off at a gulp, just as if he were trying to amuse the spectators by his antics ... now this affection arises from some humor falling on the nerves, and such irritation causes the spasm." (78) At the close of his book Sydenham states, "And this is about the sum of all I know respecting the cure of diseases, up to the day on which I write—namely, the 29th September, 1686." From that day, Thomas Sydenham never wrote again and he died on December 29, 1689 in Pall Mall. He was buried in St. James Church, Westminster. Much later, in 1810, an epitaph was written on his tombstone, which qualified him as "a physician famous for all time;" The disease he described so well is now known everywhere as Sydenham's Chorea.

This original work was soon followed by the publications of theses on chorea, which added more details. Notable amongst these are the works of Richard Mead in 1751 (47), Ewart in 1798 (22) and Cullen in 1785 (14). Most essays were published in German (76) and until 1810 the knowledge of this disease had not reached France. The man responsible for popularizing chorea in France is E. M. Bouteille, who gives a very full and

accurate historical study of the subject (5). Besides a good clinical description of the disease, he also attempts a classification. He is probably the first man to have properly recognized the association of chorea with rheumatism although the credit for this is often given to Germain Sée, whose mémoire is a model of thoroughness (70). The great clinicians Charcot and Romberg and the school of Guy's Hospital in London contributed greatly to the better understanding of chorea and sealed its importance with their stamps. To conclude the early history of this disease, mention must be made of Roger, who, in 1866, first noticed the association of rheumatism, chorea and endocarditis (68).

Meanwhile, without much notice, Francis de la Böe, better known as Sylvius, had described tremor at rest and Gaubius in 1751 had demonstrated the possibility of propulsive movements. Hughes in 1846 and G. Sée in 1850 had separated the acute from the chronic forms of chorea. By this time the confusion over terms was complete. In the first edition of his "Practice of Medicine" in 1842, Dunglison gives 15 synonyms for the same disease (19).

In his "Leçons du Mardi" for the year 1888, Charcot makes a point to distinguish between chorea and tics. "Entre le tic et la chorée, il y a un abime; ne l'oubliez pas, car il s'agit là d'affections auquelles on donne quelquefois, bien à tort, le mème nom et dont le pronostic est bien différent." (10) The remark is of importance because there had been much confusion over some atypical forms of "chorea." As we have seen, Bouteille in 1810 had already described pseudo-choreas and soon afterwards Itard reviewed the subject of abnormal convulsion of the face and limbs (36). Tics are "an abnormal and conscious convulsive movement, resulting in the contraction of one or more of the muscles of the body, reproducing, most frequently in an abrupt manner, some reflex or automatic action of common life and generally controlled by will" (Dictionnaire Encyclopédique Guinon). They can be simple and form the group of Habit Spasms which S. Weir-Mitchell wrongly calls "habit chorea" or they can be generalized with electric-like jerkings. Their name "Electric Chorea" is unfortunately a misnomer for it should be used only to describe a peculiar disease reported in Lombardy in 1846 by Dubini and manifested by spasmodic movements and shock-like muscular contractions progressing rapidly to palsy and muscular wasting. It is thought to be due to some form of malaria.

Chorea was also confused with the "Saltatoric Spasms" of Bamberger, described in 1859, which were characterized by clonic-spasms of the legs when the patient attempted to stand and caused springing or jumping movements. To be complete one would have to include amongst the diseases leading to the confusion the coordinated tics of children: head nodding, head banging and Rubinowitch's "Krouomania" which came to be recognized at about that time. But the most interesting study in differential diagnosis was done by Gilles de la Tourette in 1884, when he described a form of disease marked with explosive utterances of words or sounds and the existence of fixed ideas such as coprolalia, echolalia, arithomania and auditory hallucinations. In a historical "Tour d'horizon" he compared his "maladie des tics convulsifs" to the "jumping" seen in Maine by Beard (3) the Latah of Malaisia and the Myriachit of Syberia which Hammond had reported (27).

### JAMES PARKINSON

While the limits of chorea were being fixed through a multitude of papers, a new disease was isolated by a humble practitioner, perhaps better known to his contemporaries for his political pamphlets and his studies of anthropology.

James Parkinson was born in Hoxton, England on April 11th, 1755. His father, John, had practiced medicine at No. 1

Hoxton Square for years and was amongst the first physicians to become a Diplomate of the Company of Surgeons after it had separated from the Company of Barber-Surgeons. He died in 1784 at the age of 59 (49).

James was the eldest of three children and like them, was very religious. He studied his medicine as an apprentice to his father and was always interested in the mysteries of chemistry (46). In 1780, Dr. Hugh Smith of Hatton Street had written "An Essay on Nerves" (74) in which he stated that the nervous fluid was nothing more than air. The young Parkinson was prompt in answering with his first monograph, "Observations on Dr. Hugh Smith's Philosophy of Physics." The urge for controversy and the absolute honesty of purpose which were to characterize every step of his life had already been apparent in this, his first essay. The next year he married Mary Dale from whom he had six children. In 1785, he went away to study under the great John Hunter and learned to observe the patient for the best clues to diagnosis.

His career has many aspects and shows the versatility of a great man. As a politician, James Parkinson was a fighter. He wrote constantly under the pseudonym of "Old Hubert" on various subjects. During the French Revolution he was a pacifist and the titles of his pamphlets reveal his line of thought. In 1794, "Revolution without Bloodshed" created much controversy and he was even brought to trial for an alleged plot against the King. His feud with Edmund Burke is famous and still remembered. Parkinson advocated representation of the people in the House of Commons, he asked for annual parliaments and universal suffrage. He became a member or founder of the London Corresponding Society and the Society for Constitutional Information. As a social reformer, James Parkinson was also very active. He was a medical assistant in the Royal Humane Society and it was while working for this organization that he had the occasion of studying the methods of resuscitation of drowned children and the effect of lightning on men. He wrote a number of popular books to be used in the households: *Medical Admonitions for Families* (60) appeared in 1799, *The Villager's Friend and Physician* (58) in 1800, *The Way to Health* in 1802. He became very active in church work and asked for some reforms on the handling of trusses (55). After a sad experience in which he was accused of committing a sane person to the hospital to the benefit of her family, he asked for improvements in the laws for commitment of the insane (56). He was also a strong supporter of isolation for fever cases.

James Parkinson was probably best known to his contemporaries for his work on the Fossils of England. He was one of the founders of the Geological Society of London in 1807 and his towering work on the *Organic Remains of a Former World* which appeared in three volumes between 1804 and 1811 is considered a landmark in the history of British Paleontology. With his friend, Gideon Mantell, who later was to become famous in the same field, he travelled far and wide in the search for rare fossils.

As a physician, Parkinson was no less of an astute observer. In 1799 he published his *Medical Admonitions* (60) and prepared his *Chemical Handbook*. (59) Like others before him, Sydenham in particular, he suffered from and wrote on gout (57) and was interested in many diseases. In 1812, he reported and described the postmortem of a case of perforated gangrenous appendicitis with peritonitis in a boy five years of age. This is believed by Shepherd (73) to be the earliest reference to the disease in English Medical Literature.

The work for which he is best known in the medical world is the *Essay on the Shaking Palsy* (61) which he published in 1817. It is a remarkable rendering of concise information and an almost complete description of a hitherto unrecognized entity. He

was 62 years of age at the time of this publication. It is of interest to note that he described the typical tremor, the festination, the masked facies, the classical gait, but he did not mention the rigidity so often found in this disease. He did not study the pathology of the malady but supposed that it was "in the medulla spinalis of the cervical region, its membrane or the containing Theca."

Parkinson was rewarded with a few honors before his death. He was a member of the London Medical and Chirurgical Society, a Fellow of the Medical Society of London and in 1822, he was the first physician to receive the honorary Gold Medal of the Royal College of Surgeons of England. When he returned to his Maker on December 21st, 1824, he had lived a full and rich life.

The story of the disease which bears the name of James Parkinson will be marked by many important contributions. In the years that follow, various types of familial and senile tremors will be described and the term "Parkinsonism" will be applied to maladies closely related. We know of an idiopathic, a post-encephalitic and an arteriosclerotic form, thanks to the studies of Von Economo (21), Critchley (13), and Keschner (39). In 1911, Willige (86) postulated that there existed a juvenile form of paralysis agitans, quite different from the presenile type of Parkinson. The description of this disease and of its pathological entity was the work of Ramsay Hunt in 1917, who reported on a progressive atrophy of the globus pallidus (33) and quoted both Willige and Oppenheim. Ludo Van Bogaert (4) helped later to understand the nature of this disease and to classify it amongst the other types of Basal Ganglia involvement. The role of the great Encephalitis Epidemic of 1918 to 1928 will be told later but it must now be stated that it constitutes the real landmark of the modern approach to the problem of Paralysis Agitans.

### HUNTINGTON'S CHOREA

Meanwhile the new world was awakening to the fact of scientific medicine and the hardy pioneers took more time off from their overpowering practice to observe and record odd forms of diseases. Piece after piece of the story of chronic familial chorea was told leading to the classical description by George Huntington in 1871. Dunglison (19) in the first edition of his *Practice of Medicine*, published in 1842, is the first to call attention to this peculiar entity. He states that he had been consulted by a young medical friend in regard to the nature of a singular convulsive affection and he cites a letter dated May 5th, 1841, written by Dr. C. O. Waters from Franklin, N. Y.

The Reverend Doctor Charles Oscar Waters was born in Franklin, Delaware County in 1816. From his boyhood, he was a wanderer in search of health and religion. He studied at Williams College from 1834 to 1837 but received no degree and then decided to go to the Delaware Literary Institute as assistant teacher and then to Belvedere, New Jersey, as principal assistant to Rev. I. N. Candee (6).

Man of many talents, he studied for both the ministry and medicine. In 1839 he joined the Medical Department of Columbian University in Washington, sponsored by the Hon. Silas Wright. He then went to Philadelphia, where he graduated from Jefferson Medical College in 1841. He must have sent his letter to Dunglison upon graduation from medical school and in all probability the cases he observed were from Westchester County, New York. He gives a fairly complete description of the disease "common" as he says "in the southeastern portion of this state (New York) and known among the common people as 'the magrums'." He notes the hereditary character and observes that it differs in several respects from ordinary chorea. "First, it rarely occurs before adult age. Second, it never ceases spontaneously. Third, when

fully developed, it wants the paroxysmal character."

It is of interest to inquire into the origin of the word "magrums". Waters, himself, wonders how it could be a corruption of megrim or migraine, for there is absolutely no relationship between the disease and any type of hemicrania. It probably derives from the Dutch and the term, not mentioned in the dictionary, is used to imply restlessness or nervousness and would be about equal to our own "fidgets."

After this claim to medical fame, which was never taken up, Dr. Waters traveled to Iowa, where he practiced for some 15 years in Muscatine. He married in 1848, was editor of the Muscatine paper for one year and a member of the Iowa Medical Society until he became a minister in the Presbyterian Church. He moved to Chicago to become trustee of the Chicago Theological Seminary in 1880. During the great fire of 1871, his home was completely burned. He died in 1892, having contributed to the world a model life, and to medical science, one letter.

In his third edition, published in 1848, Dunglison mentions another similar report (20) "In an inaugural dissertation, presented before the Faculty of Jefferson Medical College, of Philadelphia, by Charles R. Gorman of Luzerne County, Pa., the writer states that this affection prevails also in other portions of the country. According to him, it seems to be circumscribed by neighborhood boundaries, and to be confined to sections of the country, the inhabitants of which are intimately connected in their social or business relations." The original thesis of Dr. Gorman was destroyed in the tearing down of the old Jefferson Medical College, where he had studied, and probably will never be known in its details. Charles Rollin Gorman was born August 4, 1817 at Barkhamsted, Connecticut. Before entering the profession of his father, he had taught school at Pittston, where he eventually settled to practice. It is interesting to note that like his predecessors, Parkinson and Waters, Gorman was a man of many fields. He was a member of the Odd Fellows and a Past Master in St. John's Masonic Lodge of Pittston. He became first president of Pittston Library Association and a vestryman in St. James's Episcopal Church. The group of cases he reported would now be classified within the "Wyoming branch," (7) (Wyoming County, Pa.)

The next mention of the new disorder is to be found in the "American Medical Times" of 1863 in an article under the name of Dr. Irving W. Lyon, who was born at Bedford, Westchester County, N. Y. on October 18, 1840. His father was Ruling Elder of the Presbyterian Church and the young Irving graduated from the University of Vermont in 1862 and from the College of Physicians and Surgeons in 1863. After a short stay as Surgeon in the Army, he became demonstrator in Anatomy at Berkshire Medical School and soon was a member of the House Staff of Bellevue Hospital in New York. It is probably from there that he sent his article on chorea (44) in which he mentions the chronic familial form which he had observed in Bedford and Connecticut, where he became Medical Director of the Hartford Life & Annuity Insurance Company until his death. His hobby was the collecting of antiques and he published a book on this subject, "The Colonial Furniture of New England." He died on March 4, 1896.

Someone once said that "genius is an infinite capacity for hard work" and this is probably the best qualification applied to the life of Dr. George Huntington. But if he rose to fame and now has his name attached to a disease, it is the result of cumulative work by many others, particularly his father and grandfather. It is also, of course, the result of his own inquiry into the mysteries of medicine and of his sound judgement. George Huntington was born in East Hampton, Long Island on April 9, 1850. His father, George Lee, was a physician and so was his grandfather, Abel, who

had settled in the same village in 1797. The grandfather, who probably was the first to observe the cases of adult chorea, but never reported them, was a well-known civic leader. He was New York State Senator in 1821 and he served two years as a congressman under President Andrew Jackson.

Huntington was only eight when he saw the first cases of "that disorder" as it was called by the natives. In 1909 before the New York Neurological Society he said, "I recall it as vividly as though it had occurred but yesterday. It made a most enduring impression upon my boyish mind, an impression, every detail of which I recall today, an impression which was the very first impulse to my choosing chorea as my virgin contribution to medical lore. Driving with my father through a wooded road leading from East Hampton to Amagansett, we suddenly came upon two women, mother and daughter, both tall, thin, almost cadaverous, both bowing, twisting, grimacing. I stared in wonderment, almost in fear. What could it mean? My father paused to speak with them and we passed on. Then my Gamaliel-like instruction began; my medical education had its inception. From this point on, my interest in this disease has never wholly ceased." (34)

This statement is true, for from the moment he finished his classical education, Huntington read books after books on medicine, worked with his father and graduated, then only 21, from the College of Physicians and Surgeons of Columbia University, with a thesis on opium. That summer he returned to East Hampton to study especially the cases of chorea in his father's practice and wrote a paper which his father corrected. In 1871, he went to Pomeroy, Ohio, to practice Medicine and was invited by the "Meigs and Mason Academy of Medicine" of Middleport to give his paper on chorea. The text of the lecture appeared in the "Medical and Surgical Reporter of Philadelphia" on April 13, 1872. At the end of what Osler calls an everyday paper on chorea, he states:

"And now I wish to draw your attention more particularly to a form of the disease which exists, as far as I know, almost exclusively on the East End of Long Island. It is peculiar in itself and seems to obey certain fixed laws. In the first place, let me remark that chorea, as it is commonly known to the profession and a description of which I have already given, is of exceedingly rare occurrence there. I do not remember a single instance occurring in my father's practice and I have often heard him say that it was a rare disease and seldom met with by him.

"The hereditary chorea, as I shall call it, is confined to certain and fortunately a few families, and has been transmitted to them, an heirloom from generations away back in the dim past. It is spoken of by those in whose veins the seeds of the disease are known to exist, with a kind of horror, and not at all alluded to except through dire necessity, when it is mentioned as 'that disorder'. It is attended generally by all the symptoms of common chorea, only in an aggravated degree, hardly ever manifesting itself until adult or middle life, and then coming on gradually, but surely, increasing by degrees, and often occupying years in its development, until the hapless sufferer is but a quivering wreck of his former self.

"It is as common and is indeed, I believe, more common among men than among women, while I am not aware that season or complexion has any influence on the matter. There are marked peculiarities in this disease; 1, its hereditary nature, 2, a tendency to insantiy and suicide, 3, its manifesting itself as a grave disease only in adult life." He then goes on to prove each of the above points. (35)

Very few descriptions of diseases ever appeared in such a concise and precise manner. And Huntington was only 22 when he wrote it! In 1884, he married Mary Elizabeth Hackard and returned to East Hampton, L. I. Because of severe attacks of spasmodic asthma, he had to limit his practice

and finally he moved to La Grangeville, N. Y. Mild-mannered, easy-going, a lover of fishing and hunting expeditions, he was the model of the devoted and generous country doctor. He moved successively to Asheville, N. C. and to Hopewell Junction. He became President of the Dutchess County Medical Society in 1888 and in 1898 honorary member of the Brooklyn Society for Neurology. He was to die in 1916, at the age of 66.

Despite the previous reports by Waters, Gorman, Lyon, and Dunglison, Huntington's paper was the first complete description of the disease and it had the good fortune of being abstracted in German by Kussmaul and Nothnagel (41) in 1872. Soon the disorder became recognized in various parts of the world and the name "Huntington's Chorea" was found in articles by Perett in 1885 and Hubert in 1887. Osler stamped the final seal of approval in his monograph "On chorea and choreiform affections" in 1894 (53).

By 1908 the disease had become so well-known that a special issue of "Neurographs" was devoted to a bibliographical and biographical review. Smith Ely Jelliffe submitted a preliminary report (38) of his investigations in which he recognized three groups of families: Group I or East Hampton Group including the cases of Huntington, Group II, or Bedford Group with the cases of Browning and Waters and finally Group III or Wyoming Group, collecting the families of Sinkler (1889) and Gorman.

Frederick Tilney (79) made a special study of the Bedford Group and traced the disorder back to the "P" family in 1777. This family was related through marriage to the Welles family, whose head was Governor Thomas Welles (1598–1660) who had married a certain Miss Hunt from England. But the classical description of the History of Huntington's chorea is told by P. R. Vessie in 1932 and traces the stain 300 years to the Village of Bures in England in 1630 (81).

In that year the famous John Winthrop fleet left England for America with about 700 passengers. Most of these came from towns and villages of Suffolk County. It must be remembered that the popular sport of witch-hunting was prevalent in those days of old England. Strangely enough, whole families of Bures and vicinity were branded as witches, tried or considered mad. Many were shunned by their neighbors and it is not surprising to find some of these miserable people amongst the passengers for the new world. The most famous of these were two brothers Wilkie and Nichols (fictitious names). Upon arrival into the colonies, Wilkie, a carpenter, was arrested for disorderly conduct and illegal actions. It is known that in 1643, his wife was mistress of a licensed "house of entertainment" in Boston and that he, himself, died in 1658.

Their daughter, Priscilla, married a certain Mulfoot (or Mulford) and moved to East Hampton, Long Island. There is no doubt that they are at the origin of the cases described by Huntington.

Their granddaughter, Elizabeth, was tried, convicted and then pardoned as the celebrated Groton witch in 1671. In the proceedings of her trial it is noted that she had "violent motions and agitations of her body."

The other member of that family, Nichols, brother of Wilkie, brought his wife, Ellin, from Bures. She came from a family known to have this disorder and later was tried for witchcraft in 1653 and hanged. As if to prove the principle of heredity, the granddaughter of Ellin was also tried for witchcraft in 1692 but by this time the courts were more lenient and she was pardoned.

On the same ship that carried Wilkie and Nichols came a man named Jeffers, who was a magistrate of sorts and had married, despite the advise of his parents, a girl from a choreic family. His eldest son, was sentenced on a charge of bestiality and was given two public whippings. The descendents of this man have many a choreic in their

midst. The best known is probably Jefferson, one of the first settlers of Greenwich, Conn. This city was well known for its immorality and libertinage and it is not surprising to find Jefferson as one of the public officials. Unfortunately, he married the daughter of Nichols and Ellin, mixing in the same family the stains of two choreic sources. As we have just seen, many of the descendents of the unfortunate passengers of the Winthrop fleet were tried and often convicted of witchcraft. It is hard for us to understand the state of mind that led to such orgies of execution in the early days of New England. Charles S. Potts in 1920 tried to analyze the witch craze in Salem in 1692 (64) and could only ascribe it to hysteria, ignorance and Puritanism. One has only to remember the disgrace of Little Rock recently and the meetings of the Klu Klux Klan to realize that such an evil is not yet ready to disappear.

The victims of Huntington's chorea were, through the strange sight of their writhing and jumping motions, well suited to be considered witches or sorcerers. "Their contortions were interpreted as the presence of the devil changing him to animals.... It was believed that the weaving motions, jerking backward and forward of the head, peculiar grimacing and twitching, puckering of the lips, squirming shoulders, spasmodic movements of the chest and diaphragm and the involuntary jerking of the hands, arms, feet and legs, represented the suffering of Christ during Crucifixion; and that this affection was a curse inherited by these sad choreics from their forefathers for having dared to derisively pantomine the Saviour." (81)

Huntington's chorea is becoming increasingly rare now, because of the ostracism attached to this disease and better awareness of its hereditary pattern.

### ATHETOSIS

We leave now the story of chorea to consider the work of another American physician, who described a new disease: Athetosis.

William Alexander Hammond was born in 1828 in Maryland, the son of a physician. Upon graduation from Medical School, he entered the U. S. Army as Assistant Surgeon. He served some seven years and was a witness of many campaigns against the Indians in the Southwest. Because of his health, he had to resign and then travelled to Europe studying the organization of military hospitals. Upon his return, he became interested in various experiments on questions of physiology and chemistry. With considerable courage, he carried out most of these experiments on himself, a habit which he kept for the rest of his life. His first paper on "The nutritive value and physiological effects of albumen, starch and gum when singly and exclusively used as food" won him first place in a contest by the A.M.A. and made him known to the medical profession. He was a friend of Silas Weir-Mitchell and with him, he made serious studies of poisons and snake venoms. In 1860, he accepted the chair of anatomy and physiology at the University of Maryland (28).

While at the University of Maryland he carried out important work on urea, uremic intoxication and the excreta in urine. All these papers were published under the title "Physiological Memoirs" which he dedicated to Weir-Mitchell.

He returned to the Army as assistant surgeon and, despite the fact that his name was far down the list for promotion, President Lincoln chose him, at 34, to become Surgeon General. This was in 1862. The young Hammond, who had a very energetic character, did not lose any time. On May 21, 1862, he announced his intention to establish an Army Medical Museum (75) and to this effect he asked for, and obtained, better reports on casualties, operations and statistics by his medical officers. This museum became in 1949 the "Armed Forces Institute

of Pathology," and holds a fabulous collection of pathological specimens.

In June of the same year he started the work that led to the "Medical and Surgical History of the Rebellion," a treatise of great value to the scholars. Through tenacity and long arguments with Secretary Stanton, he obtained the formation of the Library of the Surgeon General's Office. Later the Library started the publication of its famous "Catalogue" which has been discontinued only recently at the letter "M" of the 4th Edition. The services rendered to medical science by this catalogue are impossible to measure.

His efforts also involved the establishment of an Army Ambulance Corps and a review of the system of medical supplies and laboratories in the Army.

But, in 1863 his strong personality clashed with that of the Secretary of War, Stanton, and he was brought to court-martial. In a trial by a "packed court" he was found guilty of irregularities in the purchase of medical supplies and dismissed from the Army in 1864. Fourteen years later, an Act of Congress reversed the verdict and completely cleared him. He was again made a Brigadier General. During his stay in the Army, Hammond published a *Treatise on Hygiene*, *Lectures on Venereal Diseases*, and *Military, Medical and Surgical Topics.*

The dismissal from the Army did not stop Hammond's career; it only made it more active. Within five years he had established himself as a neurologist in New York and in 1871 published the first edition of his *Treatise on the Diseases of the Nervous System*. This book, written in an easy flowing style was so successful that it knew nine editions within a period of 25 years besides numerous translations in foreign languages.

Hammond became the editor of many journals among which were the "Quarterly Journal of Psychological Medicine and Medical Jurisprudence", the "New York Medical Journal", and the "Journal of Nervous and Mental Diseases." He became interested in Spiritualism on which subject he wrote a book, and in 1883 he published "A Treatise on Insanity" and "Sexual Impotence in the Male."

At the age of 60, he decided to relinquish his practice and he moved to Washington. This last period of his life is not known for any particular scientific achievement except for some work on "Animal Extracts." He was to die in 1900. He had been, besides his talents as an organizer and physician, a sound literateur and a superb teacher (16).

It is remembered that Parkinson, in 1817, quoted Linnaeus on an affliction involving continued distortion of the limbs without affliction of the mind. It was known as hieranosos or "Morbus Sacer". He cites a report by Macbride in 1772. It had been observed for a long time that flaccid hemiplegia was often followed by spasticity. In young patients after a certain interval, the fingers could relax at the joints and the hands were seen to close and open at intervals. The fingers then wandered from over-extension to over-flexion. In a classical description of "Cortical Hemiatrophy", in 1827, Cazanvieilh first mentioned these strange movements (9). They were known under the names of "spasmoparalysis" or "spastic-contracture" until 1871 when Hammond first applied to them the term athetosis, from the Greek Ἀθετος: without fixed position (27). He described two cases, one of which belonged to Dr. J. C. Hubbard of Ashtabula, Ohio, who had sent him his report on January 11th, 1870. The disorder "is mainly characterized by an inability to retain the fingers and toes in any position in which they may be placed, and by their continual motion." With amazing foresight he predicted that the responsible lesion would be found in the striatum.

Unfortunately even his friend Weir-Mitchell did not recognize the importance of this contribution for, in 1874, he described some post-hemiplegic movements as "hemichorea" (83). Two years later, Gowers re-

ferred to the same phenomenon as "mobile spasm" (24). Gradually, however, Hammond accepted a wider use of the term and it became standard definition. Due credit to Hammond was finally given by Greidenberg in 1886 (25). It was soon realized that some jerky movements were associated with the slower changes in posture and the term choreo-athetosis is now in more common use.

The movements recognized by Hammond, Weir-Mitchell and Gowers had also been described earlier in cerebral diplegia by Little (43) in 1862. He definitely stated, "In a few cases a distinct resemblance to severe chorea is perceptible" (p. 303). But the first adequate description of the condition now called "athétose double" (or double athetosis) is given by Clay Shaw in 1873 under the title "On Athetosis, or Imbecility with Ataxia" (71). He mentions difficulty in walking, movements of the hands and feet which he associates with athetosis, and movements of the muscles of the head, neck and face. The same year other reports by Allbutt and Purdon came to be known and a complete study was made by Oulmont in his thesis of 1878 (54). According to this author, athetosis can be found in all four limbs, but it is always present in the hands. In 1888, Déjerine and Sollier (18) described the first case of infantile bilateral athetosis and a few years later, Audry (2) collected some 79 cases from the literature. He already was able to isolate three forms: cerebral, medullar, and peripheral.

### EARLY PATHOLOGICAL STUDIES

The next important step in the story of athetosis is the description by Anton of Graz in 1896 of the striatal lesion in this disease (1) which can be considered the first report on the pathology of the extrapyramidal system. The tremendous work of Oppenheim and mainly of the Vogts will establish within a few years a very solid pathological basis of understanding for these diseases. The first breakthrough is the description in 1911 of the "Etat Marbré" or "status marmoratus" (51) which led to the concept of a "pure striatal syndrome." (82)

The life of the Vogts is interesting for it is another example of the close collaboration of a husband and wife team in the study of medicine. Cécile Mugnier was born in Annecy, France, on March 27, 1875. She studied medicine, graduating when very young, for in 1898 she was with Pierre Marie at the Bicêtre. While there, she met her husband, Oskar Vogt-Dieckmann, who was studying neurology at La Salpétrière under Déjerine. Born on April 6, 1870, he was the son of a Lutheran well respected for his liberal views. Oskar was already known in the medical world when he met Cécile. He had studied philosophy with Ferdinand Tonnier, medicine under Ernst Haeckel and Max Fürbringer, psychiatry under Otto Binswanger. Then he went to Zürich to work with August Forel and afterwards, in 1895, with Flechsig.

After one year in Paris, he left Déjerine and returned to Berlin to set up his own Department of Neurology. There Cécile came to write her thesis, fell in love and married him. In 1902, his department was incorporated into the University of Berlin. So successful was he that, in 1915, the Kaiser placed his laboratory under his protection and the "Kaiser Wilhelm-Institut" was born. Financial support came from the famous Krupp family. The growth of the Institute was such that a new one was built in 1931.

The scientific interests of the Vogts have covered many a field. From brain-psyche relationship to functional localization, they followed their pursuit in the new sciences of cytoarthitecture and myeloarchitecture. Their assistant, Brodmann, is now well known for his famous map of the cortex which appeared in 1907.

Cécile particularly became interested in the pathology of the striatum and published her description of "athétose double" in 1911.

The first case studied had been a patient of their friend Oppenheim. She was a 23 year old girl with strange movements. The diagnosis of hereditary pseudo-bulbar palsy had been proposed because the mother was known to be similarly affected. The study of the brain revealed bilateral atrophy of the striatum. Her second case had been referred by Dr. C. S. Freund of Breslow. In this brain, she found foci of myelinated fibers in the striatum which she described as "Etat Marbré."

In 1924, Oskar Vogt was invited to Moscow to study Lenin's brain and to set up a Brain Research Institute. In 1929, he described the unusual features of that brain.

Unfortunately, in 1937 the Vogts, because of their political affiliations, had to resign from the Institute but they were permitted to name their successors. Hugo Spatz became director, with Hallervorden as chief of the Department of Neuropathology.

But the Vogt's love for research could not be stopped. With the help of the Krupp family, they built a private institute for Brain Research at Neustadt and at 80 were still working every day.

### MISCELLANEOUS DISEASES

With the impetus of such a wonderful team and improved methods, new varieties of chorea became known. In 1927, J. P. Martin described hemichorea resulting from a focal lesion of the brain, which he called the "Syndrome of the Body of Luys" (45). This was not the first description and Martin himself found 21 studies of scientific value. Greiff, in 1883, Canfield and Putnam in 1884, and others described cases in which the Body of Luys was destroyed. It was Martin's lot to isolate a syndrome from these observations. It usually consisted of violent chorea of the opposite side of the body, with unusual involvement of the shoulder and hip, and therefore with movements of very wide amplitude. The face was much less affected than one would expect and there was usually a mental disturbance. Death occurred in a few weeks.

Involuntary movements affecting the limbs unilaterally and sometimes both sides of the face have been described as Hemiballismus. The term is said to have been used by Kussmaul, but Whittier in 1947 (85) has been completely unable to find any reference to it in his published works. Probably the first mention can be traced to an inaugural dissertation from the University of Vienna by Johann V. Pfefferkorn in 1833. The title of his thesis is "De Ballismo" but he calls the disorder chorea Sancti Viti and states, "One does not come across traces of this disease in the writings of Hippocrates or in the early doctorate theses, unless one is willing to consider the condition scelotyrben as ballismus" (63). Pfefferkorn, himself, states also that the word was used constantly by his master, Wilhelm Gottfried Plouequet (1744–1814) who also liked "choreomania."

Five years later, Langer also wrote a thesis on the subject (42) and he used the term ballismus to mean "to jump, to dance and above all to throw, particularly to throw back and forth, especially the legs." The disease must be particularly rare for in 1953, Malcolm B. Carpenter was able to review only 41 cases from the literature (8).

In advanced age, a condition known as "senile chorea" had long been recognized. Huet in 1888 (32) and Gowers were convinced this was a variant of Sydenham's chorea but following Osler (53) most modern writers consider the condition a form of the hereditary chorea of Huntington.

The literature mentions numerous cases of choreic movements associated with toxemia of pregnancy, mental deficiency or other conditions but the name of no one particular author is associated with this.

Of interest, despite its rarity, is a form of familial paroxysmal choreo-athetosis reported by L. A. Mount and L. S. Reback in 1940 in which strange attacks of abnormal movements occur in otherwise healthy in-

dividuals (50). In describing this disease the authors were able to show that the drinking of alcohol (definitely stated as "Whiskey U.S.P."!) could produce one of these attacks. This same observation is true for other types of familial tremors where alcohol is known to have marked deleterious effects.

"Double athetosis," as we have seen, can be found in cerebral diplegia and most frequently in association with the "Etat Marbré" of C. Vogt. But other syndromes have been described where the course is steadily progressive. These diseases are extremely rare but mention of their existence must be made in order to better understand the descriptions of dystonia musculorum deformans and of hepato-lenticular degeneration.

The first of these bears a striking resemblance to the juvenile types of paralysis agitans mentioned above. It is the "Status Dysmyelinisatus" described in 1919 and 1920 by Cecile and Oskar Vogt. The two cases they reported had athetosis in the early months of life which gradually changed to a more generalized rigidity. The first patient died at ten, the second at 13.

Two years later, the neurologists who were to replace the Vogts at the Kaiser-Wilhelm Institut reported a progressive disorder characterized by rigidity, mental deterioration and athetoid movements in five sisters of a family of 12. Hallervorden and Spatz whose names were given to this syndrome were especially struck by the brownish coloration of the globus pallidus and substantia migra without atrophy or softening (26). Other such families have since been reported in the literature.

During a famine in China in 1925, Woods and Pendleton (91) had the occasion to observe a sudden epidemic of torsion spasm and rigidity which improved in some but which became progressive in others and eventually led to death. Fourteen people were affected with this strange disease that is probably related to the Hallervorden-Spatz Syndrome.

To be thorough, one would have to mention the choreo-athetosis encountered in the progressive rigidity described by Pelizaeus and Merzbacher but the other features of this disease, nystagmus, incoordination, ataxia and spasticity are much more important and would lead us to classify it elsewhere.

Finally, Creutzfeldt (12) and Jakob (37) described a syndrome characterized by cortico-striato-spinal degeneration and sometimes called "spastic pseudosclerosis." It included Parkinson-like slowness of movement with tremor and gradual development of weakness of limbs starting usually in middle life and accompanied by hesitating, dysarthric speech and mental symptoms of anxiety or depression.

During the last year a new disease known as Kuru by the local inhabitants of New Guinea was described by Zigas and Gajdusek who observed some 154 cases on a total population of 16,000. It is limited to the natives of the Fore linguistic and cultural group on the Eastern Highlands of New Guinea. It is characterized by locomotor ataxia, malaise, fever, coryza and a Parkinson-like facies. There is little weakness or rigidity until the end which usually occurs within six to nine months. Already studies have demonstrated a widespread neuronal degeneration (93).

### DYSTONIA

Probably the most impressive of all the extra-pyramidal disorders is the one described as torsion-spasm or dystonia musculorum deformans. The spasmodic twisting and turning, the uncontrollable movements of face and limbs, the bizarre positions of the body represent the most frightening sight to the casual observer. The surprise of an epileptic attack or the antics of an hysterical woman are nothing compared to the gymnastics of the victim of this disease. It is true that no definite lesion has been found with consistency and that probably the syndrome is not entitled

to a neurological independence. It is now believed that it is closely related to hepatolenticular degeneration but until a better understanding is reached it will have to be considered separately.

The first man to report such a disease was probably Schwalbe in 1908 (69). In his Inaugural Dissertation in Berlin, he described a sister and two brothers with progressive involuntary movements who threw their hands behind their back and would bend in almost complete opisthotonos. Schwalbe worked in Ziehen's clinic and the next year the master himself reported two other cases before the Psychiatric Society of Berlin (92). He called this disorder "tonic torsion-neurosis." It is very probable that many such cases had been previously described under the term "tetanoid chorea" of Gowers, and Wilson states that he himself had seen some in London around 1904.

In 1911, the great Hermann Oppenheim who was already famous for his descriptions and diagnosis of brain tumors, tabes dorsalis, bulbar paralysis and neuritis, coined the term "dystonia musculorum deformans" in reporting four cases of the disorder. He described the characteristic "dromedary gait" due to lordosis. Since, much work has been done on this subject but, to date, it has only added to the confusion both on the pathology and the clinical independence of the disorder.

## WILSON'S DISEASE

The period between 1900 and 1917 was extremely fertile in neurological discoveries. Great pathological studies were underway with new staining methods and improved instruments. Of all the publications which blessed the world of science, few deserve the praise and recognition that was given a doctoral thesis by a relatively young House Physician of the National Hospital, London. In 1911, at 33 years of age, Kinnier Wilson described before the Neurological Society of London "Progressive lenticular degeneration: a familial nervous disease associated with cirrhosis of the liver." His paper, a masterpiece of thoroughness and clairvoyance was published a year later and was a mere 200 pages long! (87)

Samuel Alexander Kinnier Wilson was born in New Jersey, but was brought up and educated in Scotland. His medical studies took him from the University of Edinburgh to Germany and France where he studied under Pierre Marie and Babinski. In 1904, he started in Queen Square one of the most brilliant careers in Neurology which ranked him at a par with men like Gowers, Horsley and Jackson, most of them his friends and contemporaries.

After the publication of the famous paper on what is now known as Wilson's Disease, he devoted most of his energies on what he had himself christened the "extra-pyramidal system." His papers and lectures had an uncommon literary quality where keen analytical powers and remarkable insight were evident. No neurologist can ever forget the reading of his volume *Modern Problems in Neurology* (88) or of his posthumous textbook, *Neurology* (89).

A great teacher and a man devoted to truth, Wilson himself had to recognize the pioneer work of others in the description of the clinical syndrome of progressive lenticular degeneration. The disease, which is familial, is characterized by a coarsely nodular cirrhosis of the liver associated with the occurrence of progressive tremor and/or rigidity. The tremor is usually absent during complete rest but it is considerably increased in amplitude with movements. The rigidity is also variable but is in common with that found in many diseases of the basal ganglia.

The first effort to differentiate disorders of bodily posture from multiple sclerosis was attempted by Westphal in 1883 (84). In two cases which he described, there was some tremor and disturbance of speech. He theorized that they could be attributed to "a neurosis which may, perhaps, though not very suitably, be described as 'pseudo

sclerosis'." Soon afterwards, in 1898, Strümpel revived the term in describing three cases with the same clinical appearance. The last of these, a young man of 24, had early hepatic cirrhosis (77).

The term "pseudo sclerosis" or Westphal-Strümpel Syndrome was vehemently attacked by Wilson and rejected from his syndrome, but despite this it must still be retained to qualify cases where tremor with little or no postural aberration is present.

We remember Gower's description in 1888 of "tetanoid chorea," a familial, acute, progressive nervous illness. In his paper, he mentioned the presence of cirrhosis of the liver and similar reports appeared later under the name of Ormerod (52) and Homen (30) both in 1890. Finally, in 1909, Fleischer (23) described a curious ring of golden corneal pigmentation in a case of pseudo sclerosis with cirrhosis of the liver. Seven years previously, Kayser had mentioned a similar finding and this sign was considered almost pathognomonic of Wilson's disease until recently when it was encountered in torsion-spasm. In the last few years, a metabolic disorder of copper has been found in hepato-lenticular degeneration, opening up a whole new field of studies (15).

## ENCEPHALITIS LETHARGICA

Just as the neuropathologists were beginning to describe the lesions of most of these disorders and as the physiologists, under the impulsion of Kinnier Wilson, were involved in understanding the functions of the extrapyramidal system, of the "old and the new motor systems," there occurred in most of Europe a pandemic of encephalitis which was to create the impetus for a tremendous amount of research. The epidemic of encephalitis lethargica, as it was known, came in the wake of a terrible pandemic of influenza which did considerable damage throughout the world (21).

The disease appeared in Rumania in the Spring of 1915 and the first few cases were reported by Urechia who observed mainly the ophthalmoplegic and hyperkinetic forms. Some isolated cases were probably seen among soldiers near Verdun in the last few months of 1915 by Cruchet and again in Rumania by Marinesco but the first real epidemic was reported during the Winter 1916–17 in Vienna. The man who published the first account of this disease and who is forever associated with it is Constantin Baron Economo von San Serff. He was born in Braila, Rumania, in 1876 and lived in Trieste until he went to Vienna to study engineering (at his father's request) and then medicine. He worked with Nothnagel and then went to Paris to benefit from the teachings of Magnan and Pierre Marie. After a short stay with Bethe in Strassburg and Kraepelin in Munich, he returned to Vienna in the clinic of Wagner von Jauregg. It is interesting to note that he was passionately interested in aeronautics, became a balloon and then an aircraft pilot. His energy led him to organize the Vienna airports and the Austrian aeroclub, all the while studying the physiology and anatomy of the midbrain (40). He is mainly known for his studies on encephalitis lethargica but his best work is probably the atlas on the cytoarchitecture of the adult human cerebral cortex which he published in 1925. He was to die in 1931, shortly after becoming director of the brain research institute of the von Jauregg Clinic.

There has been some argument on the priority of von Economo's article over Cruchet's but it now appears certain that the Baron reached press at least ten days before, and anyway, his account was much more complete and descriptive. It was dated April 17, 1917. The mortality in Vienna of this epidemic was reported to be over 50 per cent. The disease was soon recognized in Leipzig by Strümpel but it remained "mysterious" in Queensland. The first few cases which appeared in 1918 in London were mistaken for Botulism until in October it was identified as von Economo's disease. The epidemic reached France in March,

1918, and was thoroughly described by Netter, Lhermitte, Claude, Pierre Marie, Vincent and Sicard. Towards the end of that year it had spread its damage to most of the world, including North America.

A recurrence took place in Italy at the end of 1919 and because of its violence rapidly spread along the Adriatic Coast to Austria. This time the hyperkinetic form was prevalent and became generalized to all Europe. 1920 and 1921 were considered pandemic years with an overall mortality of nearly 40 per cent. Sporadic cases were still met with till 1928. By that time the great sequelae which make this disease so important in our study, were beginning to appear. Parkinsonism in its new form became a common disorder and a multitude of reports appeared with the descriptions of various pathological involvement. This epidemic can truly be placed at the start of a renewed interest in the problem of involuntary movements, but it certainly was not the first of its kind in history.

The fact that influenza and encephalitis were prevalent at about the same time contributes to obscure the picture. It is quite probable that some of the tremors observed in the Middle Ages and mentioned earlier, were similar diseases. Von Economo and many others, among whom Riley stands out, have attempted to trace the history of encephalitis. Hippocrates mentioned a "Lethargus" accompanied by fever but its true nature is uncertain. In 1580 it is known that there was a bad influenza epidemic in Europe. In 1673 Sydenham reports a few cases of what he calls "febris comatosa" while in 1695 Albrecht of Hildescheim definitely described a case of sporadic somnolent-ophthalmoplegic form of this disease. Many other similar epidemics are made mention of by Ozanam (1745), Lepecq de la Cloture (1763), Grant (1775), Pfendler (1830), but the one that is best remembered is certainly the great epidemic of influenza of 1889 in Italy which was followed the next year by a peculiar disease which the natives called "nona" and which since has received much attention.

The tragedy of Encephalitis Lethargica and its sequelae renewed the search for a cure to involuntary movements. On the medical side, a host of drugs were introduced to alleviate either tremor or rigidity. The vogue of the Bulgarian treatment has now passed, but the efficacy of belladonna or its derivatives is still the same. New synthetic drugs appear every year in the hope that a breakthrough will occur but the only result at present is a long list of trade names.

On the surgical side, audacity and invention combined for a full sized attack (48). From Horsley's excision of the precentral cortex in 1890 in a case of athetosis, one can really say that all levels of the pyramidal and extra-pyramidal tracks have been assaulted. Cortical excision was attempted by Bucy and Klemme (1937), and internal capsule lesion by Browder (1948). The peduncles were cut by Walker (1949), the spinal cord by Putnam (1938), Oliver (1949) and Ebin (1949). Posterior nerve root separations were done by Pollock (1929) and sympathectomy by Gardner (1949). Finally, the basal ganglia were attacked by Meyers (1940), Spiegel and Wycis (1951), Fenelon (1950), and Guiot (1952). The latest vogue was introduced by I. S. Cooper in 1953 and involved ligation of the anterior choroidal artery which led to the refinement of chemopallidectomy (11).

But what of the results? Many are improved that a few years ago would have been miserable, many are permitted a more active life and are forever grateful... but none are cured! The cause and exact pathology of the various diseases grouped under the extra pyramidal system remain mysteries almost as deep as in the days of Sydenham and Parkinson. Many clinical varieties have been observed, many pathological studies carried out, but the suffering humanity still goes on twisting, shak-

ing, writhing, jumping and jerking when it does not want to. It is possible that the whole concept of extra-pyramidal diseases will be destroyed shortly. It is even possible that a chemical or metabolic abnormality will be found common to these entities, but until then there is still much work to be done and the physician, man above all, must know that for the present the best he can offer still is understanding, charity, hope and faith.

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# TUMORS OF THE SEPTUM PELLUCIDUM AND ADJACENT STRUCTURES WITH ABNORMAL AFFECTIVE BEHAVIOR: AN ANTERIOR MIDLINE STRUCTURE SYNDROME

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This paper deals with the psychopathology encountered in patients with neoplasms in the anterior midline structures of the brain. It is not intended to augment the casuistics of intracranial tumors posing psychiatric problems, but rather to focus upon what appears to be a characteristic clinicopathological relationship.

In discussing the clinical aspects of cerebral neoplasms it is customary to divide the changes of nervous function into two categories: (1) general symptoms and signs, and (2) focal symptoms and signs. Of course, there may be a considerable overlapping of these two divisions. Among the general symptoms, personality changes are especially prominent. They were observed as initial signs in 21 per cent of brain tumor cases by Baker (1). Mental changes as focal signs are usually considered evidence of an involvement of the frontal lobe. From the evidence presented in this paper it appears that there exists, in addition to the frontal lobe syndrome, a syndrome of the anterior midline structures of the brain.

Although this symptom-complex was first described 60 years ago, it has received little attention. For instance, it is not mentioned by Walther-Büel (19) in his extensive study on the psychiatric aspects of brain tumors. This may be due in part to the fact that it is not commonly encountered. More important, however, it appears that its neurophysiological basis has been investigated only recently.

In 1895, Ransom (14) observed a 24 year old housewife with a tumor of the septum pellucidum, also involving the fornix and corpus callosum. He was impressed by the lack of symptoms referring to an intracranial neoplasm. Instead, his patient presented a chronic "psychoneurosis" characterized by mental excitability, restlessness, and irritability. After a study of ten cases from the literature with similarly located neoplasms he reached the conclusion that, "the most characteristic clinical aspect (of tumors located in the anterior midline structures) is a gradual but marked mental change in more acute cases taking the form of an increasing stupor, in the more chronic appearing as insanity with delusions, irritability and maniacal outbursts."

It is apparent that Ransom's series constituted a heterogenous group. Some of the cases he quoted were gliomas of the genu of the corpus callosum with excessive butterfly infiltration of both frontal lobes; hence his emphasis on insanity and stupor. In those cases in which the neoplasm is restricted to the anterior midline structures, disturbances of affective behavior in the direction of increased emotionality, dominate the clinical picture, as will be shown in this presentation.

## CLINICAL OBSERVATIONS

It should be noted that none of the four cases which came to our attention was correctly diagnosed on the basis of the clinical findings. In fact, Case No. 2 was never suspected to suffer from a cerebral neoplasm. In Case No. 1 a brain tumor was diagnosed only after an ill-advised spinal tap had led to a rapidly mounting intracranial pressure. In the third case, which was under neurosurgical observation, the diagnosis of a tu-

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mor of the septum pellucidum was made. However, this diagnosis emerged as a surprise finding from a ventriculogram rather than as the outgrowth of clinical considerations. In Case No. 4 the situation was similar.

As a result of these circumstances the psychiatric data, which in our opinion are suggestive of a syndrome of the anterior midline structures, are necessarily incomplete and of a subjective nature. It is with these shortcomings and the resultant diagnostic errors in mind that the cases are reported here.

It is our hope that the histories presented will lead to future efforts to delineate and objectify the psychopathology associated with lesions of the anterior midline structures.

CASE NO. 1.

This 41 year old housewife was admitted to the hospital with a diagnosis of organic brain syndrome. The patient had been under medical treatment intermittently for 18 months. It was at the insistence of her husband that she sought medical advice in February 1955, because she had become "severely nervous." She was irritable at times, cried at the slightest provocation and proved increasingly inefficient in her housework. The family physician suspected an impending menopause and prescribed a bromide solution, which apparently relieved her symptoms to the extent that the patient regained her premorbid disposition temporarily.

Later in the course of the disease the efficacy of the bromide treatment declined and the patient again became emotionally unstable. Early in August 1956 she began to complain of dizziness and headaches. There was also occasional vomiting. At this time her husband reported that she was sometimes confused and disoriented with "thickened speech." She also became untidy about her person and was extremely careless about taking her medicine. Her husband related that she would consume large quantities of the bromide solution at one time, but then would abstain for days. Therefore bromide poisoning was suspected when the patient was admitted to the hospital.

*Physical Examination on August 25, 1956.* The patient looked somewhat older than her stated age. She appeared bewildered, but not acutely ill. Blood pressure 130/90, pulse 88, temperature 99.6. Chest, heart, and abdomen negative.

*Neurological Examination.* Fundi not visualized. External ocular movements free. Pupillary reactions prompt, the right pupil was questionably larger than the left. Remainder of the cranial nerves intact. Motor functions: Questionable weakness of left side. Oppenheim and Hoffman positive on left. Abdominal reflexes absent (Para 3). Neck supple. Romberg negative. Coordination intact. Sensory functions normal. Speech dysarthric.

*Mental Status.* Patient appeared somewhat lethargic and disinterested. At times she was confused and did not know where she was. At moments she was well oriented in all three spheres. She talked freely, with thought content centering around complaints of headaches and vomiting. A definite disorganization of thinking was noted. The patient was sometimes unable to finish a sentence. No evidence of hallucinations or delusions was elicited.

*Laboratory Data.* Blood bromide 65 mg. per cent. Blood count normal. Serology negative. Skull x-rays normal. EEG: two to three cycles per second activity over the left anterior quadrant and irregularly formed eight to nine per second activity with medium to moderately low voltage in all leads.

*Hospital Course.* A spinal tap was performed on August 27, 1956. Pressure 410 mm $H_2O$; RBC 141; WBC 4; protein 25 mg. per cent; sugar 58 mg. per cent; colloidal gold curve 1222110000. Following this procedure the patient became increasingly stu-

FIG. 1. Case No. 1. Frontal section at the level of the anterior commissure, Thionin, 1.5X. Tumor involving septum pellucidum, lower strata of corpus callosum and spreading into the corona radiata corporis callosi.

porous. She was transferred to the neurosurgical service. At that time a 4-diopter papilledema was found. As an emergency measure a ventriculogram was performed on August 28, 1956, which was diagnostic of a tumor of the septum pellucidum. The patient remained in stupor and died on August 29, 1956.

*Autopsy Findings.* The brain weighed 1480 grams. The convolutions were markedly flattened and brain tissue had fungated through two occipital burr holes. There was a bilateral uncal herniation, .7 cm. wide on the left and 1.0 cm. on the right. The cerebellum revealed a pressure cone measuring 3 cm. in length and 3.7 cm. in diameter at the base. The meninges were translucent and the basal arteries were patent.

On coronal sections the white matter of the centrum ovale was edematous. The ventricular system was not dilated. The septum pellucidum measured 2 cm. in thickness, the genu of the corpus callosum 2.6 cm. These structures appeared edematous and showed a slight yellowish discoloration. No hemorrhages were encountered here. The anterior part of the third ventricle was partly obliterated by the enlarged septum and fornices which were displaced posteriorly and caudad. Through both occipital lobes the stab wounds of the ventricular taps could be traced. In the tegmentum of the pons and mid-brain numerous petechiae and hemorrhages up to a diameter of 2 mm. were found.

*Histology.* Sections through the genu of corpus callosum stained with toluidine blue revealed an infiltrating glioma (Figure 1). The fornix columns were so completely involved that they could not be identified. The tumor extended bilaterally into the corona radiata of the corpus callosum and the subcallosal bundle to a depth of approximately 2 cm. The neoplasm consisted chiefly of bipolar spongioblasts but there were numerous foci of small undifferentiated and multinucleated giant cells. The stroma was inconspicuous and no necrosis was noted.

*Diagnosis.* Spongioblastoma with beginning anaplastic changes of septum pellucidum and genu corporis callosi with infiltration of subcollosal bundle and corona radiata.

*Comment.* This 41 year old white female had an 18 month history of "nervousness" manifested by irritability, emotional instability and lack of efficiency. During the last month of her illness general signs of a brain tumor developed in form of nausea, vomiting, and headaches. Occasionally the patient was disoriented. At the time of her hospital admission, 18 months after the onset of illness, a left-sided hemiparesis, a possible aphasia and dysarthria were noted. The patient died subsequent to a contra-indicated spinal tap which had led to increasing intracranial pressure and progressive stupor. It was only then that a severe papilledema was found.

Autopsy revealed a spongioblastoma of the septum pellucidum and adjacent areas, undergoing anaplastic changes.

CASE NO. 2

This 67 year old retired railroad worker was hospitalized for an organic brain syn-

drome. The patient had an excellent work record and apparently had enjoyed a harmonious family life. He retired in 1948 and spent most of his time at home. Later the family moved to Florida. In 1954 his wife first noticed an insidious mental change. At the beginning there were episodes of restlessness with occasional temper "flare-ups" quite uncharacteristic of him, while in the course of his illness outbursts of violence occurred. His wife believed he was having a difficult time adjusting to retirement and did not suspect mental disease. However, as the outbursts of temper and violence became more frequent, he showed increasingly inappropriate reactions to minor stresses and irritations. His wife recalls an incident during which he dropped her from the car after an argument and was found hours later roaming the streets of another city some 40 miles away. On another occasion he left the house in anger and was heard driving away. The next day he returned home on foot. His car was later located on an uninhabited island in the Gulf and the patient was unable to explain how it got there and how he returned to the shore.

The patient and his wife, upon the insistence of the family, moved back to their rural home in Ohio, because it was thought he could not tolerate the leisure of his retirement in Florida. There he began to threaten the neighbors and was frequently seen wandering aimlessly about. Consequently, the community filed a petition for detention, upon which the patient was admitted to this hospital.

*Physical Examination, October 26, 1956.* The patient was an elderly, well nourished and well developed white male who did not appear physically ill. Blood pressure 130/74. Pulse 64. Temperature 98. Chest normal. Heart: Grade I aortic systolic murmur, not enlarged. Abdomen: Liver 3 cm. below costal margin, not tender. Tortuosities and hardening of peripheral arteries were noted.

*Neurologic Examination.* Cranial nerves intact. Station and gait not remarkable. Deep tendon reflexes 1+ and equal bilaterally. Sensory system grossly intact. Handwriting: Clumsy and distorted. Romberg negative. Speech not remarkable.

*Mental Status.* The patient was unable to give any reliable information. He was confused and disoriented in all three spheres. He looked depressed, kept his head bent downward. He was circumstantial but tried to cooperate. Cognitive functions were impaired. Memory for old and recent events was extremely poor. He could not solve simple arithmetic problems. His judgment was greatly impaired and he had no insight for his condition.

*Laboratory Findings.* Spinal fluid pressure 214 mm $H_2O$. WBC 2, protein 45 mg. per cent, colloidal gold 0011112000. Blood count normal. Serology negative. Skull x-rays normal, sella turcica well mineralized. EEG: All leads reflected irregularly formed 8 per sec. medium to moderately low voltage waves. The left hemisphere leads, especially over the anterior quadrant contained poorly formed 2–4 per sec. medium to moderately low voltage waves.

*Hospital Course.* The patient confabulated freely. His behavior on the ward was characterized by agitation. He wandered about looking for lost keys; repeatedly he tried to get out to repair his car. At times he was abusive to other patients and became belligerent, especially during visits by his wife. At times he presented a staggering gait.

On November 9, 1956 he was transferred to a state hospital with the diagnosis of chronic organic brain syndrome associated with cerebral arteriosclerosis and arteriosclerotic heart disease. No medical records were available for this period. He died on December 26, 1956 from multiple pulmonary emboli. During his entire illness a cerebral neoplasm had not been suspected.

*Autopsy Findings.* The brain weighed 1,320 grams after formalin fixation. The

gyri were somewhat flattened. The meninges over the convexities appeared cloudy. The basal arteries exhibited multiple atheromatous plaques and tortuosities but were patent. There was a bilateral uncal herniation measuring .5 cm. in width. Cerebellum and brain stem were not remarkable.

On coronal sections septum pellucidum and genu corporis callosi appeared markedly thickened, the corpus callosum measuring 3 cm. and the septum pellucidum 2 cm. The anterior part of the third ventricle was completely obstructed by this enlargement but the foramina of Monroe were patent. The lateral ventricles were mildly dilated. The tumor was of firm consistency and exhibited the color of the white matter.

*Histologic Findings.* Celloidin sections through the tumor stained with thionine revealed an infiltrating glioma which involved the fornices, septum pellucidum and the genu corporis callosi. The tumor had spread anteriorally along the corona radiata into both frontal lobes to a depth of 1 cm. The cellularity varied from region to region but was most dense in the septum pellucidum. There were no hemorrhages or necrosis. Most of the tumor cells were bipolar spongioblasts. In a few centrally located areas, however, multinucleated giant cells predominated. The stroma was inconspicuous.

*Diagnosis.* Spongioblastoma of septum pellucidum and genu corporis callosi with infiltration of corona radiata.

*Comment.* This 67 year old white male had a two year history of psychic abnormalities, first manifested by disturbances of affective behavior in the form of temper flare-ups and outbursts of violence. During the later phase of the illness there was marked confusion, disorientation, and agitation. A neurologic examination two months prior to this was negative except for the staggering gait which occurred only occasionally. However, the grossly abnormal EEG at that time should have aroused suspicion of an intracerebral neoplasm with increased intracranial pressure.

At autopsy a spongioblastoma of the septum pellucidum and the genu corporis callosi was found.

CASE NO. 3

This 62 year old school teacher[2] was admitted to the hospital with a chief complaint of vertigo of three weeks duration.

The patient had been exceptionally well suited for her profession as a school teacher because of a balanced, calm, and pleasant disposition. Under these circumstances relatives were alarmed to note that during the spring of 1956 the patient showed signs of increasing irritability. She had difficulty remaining calm in the classroom and tended to become unreasonably angry with pupils. Moreover, she became subject to emotional outbursts that she could not control. The patient herself became concerned as she was unable to comprehend these uncharacteristic reactions. She had good insight and stated that the outbursts were unreasonable on her part.

Another feature of the early phase of the disease was that the patient developed a sensitivity to sudden noises. The sound of a closing door, the clicking of dishes being washed, or the ringing of a doorbell would elicit an extreme startle response in the patient. While these symptoms were disturbing, the patient did not quit teaching school until she began to suffer seriously from a memory disturbance. At first she could not recall recent events but soon thereafter she noted impairment of memory for events long passed, which seriously interfered with her professional activities. Eventually she became disoriented as to time and place and displayed episodes of confusion. Shortly after the occurrence of the latter symptoms she was hospitalized.

*Physical Examination on January 20, 1957.* The patient was a well developed, obese white female in no acute distress.

[2] We are indebted to Dr. Richard Retter of Columbus, Ohio, for permission to include this case.

Blood pressure 158/92, pulse 68, temperature 98. Chest, heart and abdomen normal.

*Neurologic Examination.* Cranial nerves intact. Romberg positive. No motor weaknesses. Tendon reflexes 1+ equal bilaterally. Gait was wobbly and unstable. There was lack of position sense in both toes. Finger-to-nose test well performed. Knee-to-heel test showed incoordination with ataxic tremor on both sides. The impression was that of a posterior column lesion.

*Laboratory Examination.* Blood count normal. EEG showed a generalized dysrhythmia with medium to slow voltage 8 per sec. activity on all leads. No focal abnormalities.

*Mental Status.* The patient was disoriented as to time and place. She confabulated freely. For instance, she declared that she remembered persons she had never seen before. The resident was identified as a former colleague of hers.

*Hospital Course.* On January 28, 1957 a beginning papilledema was found. Subsequently a ventriculogram was performed which showed a space-occupying lesion in the anterior mid-brain structures which had displaced both anterior horns laterally and the third ventricle downward and caudad.

A diagnosis of tumor of the septum pellucidum was made and the patient was operated on February 6, 1957. By transcallosal approach parts of the tumor were removed. Subsequent to the operation the patient was in critical condition with seizures involving her right side. She expired on February 8, 1957.

*Autopsy Findings.* The brain weighed 1470 grams after formalin fixation. It was symmetrical in shape. The gyri were flattened and the sulci narrowed. There was bilateral uncal herniation measuring 1 cm. in width and a small pressure cone around the medulla oblongata.

The middle third of the right first frontal gyrus adjacent to the interhemispheric fissure was partly destroyed and showed a deep conically shaped defect with a base diameter of 4 cm., and a depth of 4 cm. This defect was partly covered by coagulated blood and tissue debris. The corpus callosum was perforated by a hole measuring approximately 2 cm. in diameter. The supracallosal gyri on both hemispheres bordering this defect were superficially destroyed.

On coronal sections it was noted that the above described defect had destroyed cortical area 24 from .5 to 1.5 cm. in depth. The surrounding tissue exhibited numerous petechiae extending to the area of the second frontal gyrus. The genu of the corpus callosum, the septum pellucidum, and the fornix were fused together and involved by a tumor mass, cylindric in shape and measuring 4 cm. in diameter and 5 cm. in anterior-posterior extent. This tumor was partly hemorrhagic and extended caudad following the pathway of the fornix into the fimbria of the left hippocampus. The right hippocampus appeared normal. The fimbrial and hippocampal part of the tumor was nonhemorrhagic, but rather edematous, and of a gelatinous appearance.

*Histology.* The tumor consisted chiefly of polar spongioblasts as seen in toluidine blue sections. The tumor cells exhibited the typical elongated nuclei arranged parallel to the path of the predominating fibers. Only in the area of the septum pellucidum and the corpus callosum was some degree of pleomorphism and anaplasia noted. Here the vascular stroma was conspicuous with formation of glomerulus-like structures. In the hippocampal portion the tumor showed a rather poorly developed stroma. The brain tissue adjacent to the tumor exhibited ischemic ganglion cell necrosis and edematous necrosis of the white matter, with a rather marked glial reaction (Figure 2).

*Histologic Diagnosis.* Spongioblastoma of limbic system, with anaplastic changes.

*Comment.* This 62 year old patient had a history of mental disturbances for one year. Her symptoms began with a hyperemotionality. Later on this was followed by rather striking startle responses to unexpected

FIG 2. Case No. 3. Frontal section at the level of the posterior commissure, Thionin, 1.5X. Tumor involving fornix (F), corpus callosum (CC), and spreading into cingulate gyrus and corona radiata corporis callosi.

noises. There were episodes of temper outbursts and eventually a severe confusion and disorientation. The first signs of an organic central nervous system lesion occurred in the form of dizziness and ataxia of the lower limbs first, and were interpreted as posterior tract signs. The abnormal EEG, however, together with an impending papillary edema, aroused suspicion of a brain tumor and at ventriculography a neoplasm arising in the septum pellucidum was found which, upon histologic examination, proved to be a spongioblastoma.

In this case it is noteworthy again that the psychological symptoms preceded the onset of definite and objective neurologic deficits for almost one year.

CASE NO. 4

This 34 year old housewife[3] was admitted with a diagnosis of brain tumor. She was apparently in good health and well balanced mentally when she experienced her first grand mal seizure eight and one-half years ago in 1950 at age 25. From then on she had grand mal seizures at a rate of approximately one per month for the next two and one-half years, although she had been placed on dilantin, mesantoin, and phenobarbital.

During this period of time she had seen numerous physicians and had undergone diagnostic studies including x-rays of the skull and EEG's which reportedly were normal. The husband relates that she developed an addiction to phenobarbital slowly over the years. In 1953 she received prescriptions for phenobarbital from fifteen different physicians at the same time. She was rather careless in taking this medication, complained frequently of headaches and was most of the time in a "dopey" condition. In the spring of 1953 she was picked up by Federal narcotics agents and placed in a mental hospital in Wichita Falls, Texas. However, the attending physicians did not feel that she was a drug addict. This opinion was based upon the fact that she had no withdrawal signs and evidently had episodes of apparent "drunkedness" without any medication. She was released in custody of her husband who took all medication away from her, and the local drug stores in the community were advised not to sell narcotics to the patient.

From then on the patient did not experience any seizures for more than four years, although she took no anticonvulsants. The husband, however, noted an insidious mental change beginning around that time. The patient would call in physicians and demand injections of narcotics. If the physician would not comply with her wishes she became abusive verbally and threatened him. The husband believes that somehow the patient was still getting narcotics because she had episodes of "drunkedness" in which she would undress herself and sometimes urinate on the floor. The husband recalls two episodes during this period in which the patient became assaultive. At one time she threatened verbally to poison him and at another occasion she attacked him with a paring knife. However, on both oc-

[3] We are indebted to Dr. Harry LeFever of Columbus, Ohio for permission to include this case.

casions there was a preceding verbal argument between the two. During all this time the patient was restless and could not sit still. She was unable to take care of the house so that the husband had to employ outside help.

Since 1955 the patient has complained of headaches and tried to obtain alcoholic beverages in order to get relief. As a substitute she would drink Bromo-Seltzer or would attempt to get paregoric and similar drugs. There were frequent episodes of screaming and crying without apparent cause.

Both the husband and the mother noted that beginning approximately 1953 the patient became easily startled and would shriek at any unexpected noise. She became so fearful and easily frightened that she gave up driving about that time.

During a visit with the mother in the Spring of 1957 the mother was deeply impressed by the fact that her daughter was frequently crying for no apparent reason. She was upset most of the time and occasionally complained of unbearable headaches. She was unreasonably tempered upon occasion, but at other times she appeared depressed. Although she was highly irritable she would calm down readily and often would realize afterwards that these temper outbursts had been unreasonable.

In January, 1958, she again experienced grand mal seizures and was immediately placed on dilantin and phenobarbital. However, the seizures continued. It was then noted by the husband that following the seizures she would show a weakness of all extremities and had to rest for a prolonged period in bed until she could get up. In the meantime she and her husband had moved to another locale where the patient called in the sheriff with the unfounded idea that the husband was trying to kill her.

The seizures became more frequent and the patient again took large quantities of narcotics and drank any alcoholic beverage she could get. On several occasions she would urinate wherever she was and on one occasion she defecated and smeared her face with feces.

In May, 1958, the husband for the first time noted a limping on the left side which became worse after a seizure. By that time all physicians in the community refused to treat the patient because she became so abusive and was very difficult to manage. Therefore, the husband again had to sell his business and move to a new community. It was then that the physician who was called in noted a papilledema and referred her to this hospital.

*Physical Examination on July 23, 1958.* A well developed, well nourished, white female. Blood pressure was 94/58, temperature 100 rectally, pulse 70, respiration 16.

*Neurologic Examination.* Pupils were round and equal, and reacted briskly to light. There was no nystagmus. The optic discs showed a marked 2–3 diopter papilledema bilaterally with venous engorgement and small perivenous hemorrhages. Otherwise the cranial nerves were intact.

The gait was wide-based and spastic on the left. There was definite incoordination on the left side on the finger-to-nose and knee-to-shin tests. On holding the hands over the head the left arm drifted. The muscles on the left side were hypertonic. All muscle stretch reflexes were hyperactive, more so on the left side. A sustained achilles clonus was released on the left side. Plantar responses were flexor. Sensory functions were not impaired.

*Mental Status.* The patient was quite responsive to verbal stimulation, but her thinking processes were slow and she was somewhat confused. She was definitely disoriented as to time and had a very poor recollection of recent events. Therefore, she was able to contribute little to her past history.

*Laboratory Findings.* Serology negative. Urine contained 10 mg. of protein, blood count 13,300 WBC, 15.2 grams hemoglobin, electrolytes within normal limits. The EEG showed a generalized slowing and disorgan-

FIG. 3. Case No. 4. Ventriculogram, showing intrusion of a calcified neoplasm into the lateral ventricles.

ization with overall low voltage and a right anterior quadrant 2–3 cycles per sec. focus.

*Hospital Course.* A right-sided carotid angiogram was performed, the findings of which indicated a tumor most likely in the basal ganglia on both sides. A ventriculogram showed a slight hydrocephalus of the lateral ventricles with a tumor mass containing abundant calcium which appeared to be arising from the anterior portion of the corpus callosum with invasion into the right thalamus. The third ventricle was displaced to the left, caudad and downward with no dilatation (Figure 3).

On the basis of these findings a craniotomy was performed and a tumor mass was partly removed from the anterior part of the lateral ventricles by transventricular approach. The tumor involved the septum pellucidum and the fornix columns and extended into both lateral ventricles as well as into the corpus callosum. Approximately one-third of the tumor, having the size of 4 cm. in anterior-posterior extent, and 3 cm. in lateral extent, was removed.

The histologic examination showed a moderately cellular, well differentiated astrocytoma with abundant formation of astrocytic fibrils and large areas of calcification. Mitotic figures were not seen and vascular structures were inconspicuous.

The post-operative course was uneventful. There was a marked improvement of her left hemiplegia to the extent that she could walk again. Her coordination reverted to normal. She still complained about headache but had no seizures. On the other hand, her mental status was little changed by the operation. She was still disoriented, confused, and emotionally unstable, although somewhat less so than before surgery. Her memory for both immediately recent and long past events was poor, and she confabulated continually. Her moods were subject to sudden, moment-to-moment fluctuation. At one instant the patient was smiling and pleased, and the next moment she was morose and tearful. These rapid mood changes seemed unrelated to external stimuli. Although the patient could solve simple arithmetic problems, she failed when more complicated reasoning was required.

*Comment.* This patient had a history of seizures beginning over eight years ago and lasting for two and one-half years. After that she experienced a period free of seizures but at the same time developed signs of mental disorder. This was characterized by erratic behavior, irritability, restlessness and occasional episodes of violence and delusion, alternating with depression and crying. Undoubtedly the clinical picture has been somewhat clouded by the free use of narcotics and other nervous system depressants. During all this time the patient had intermittent periods of severe headaches which had grown almost unbearable at the time the seizures recurred in January 1958. From then on the course of her illness became rapidly progressive with episodes of Todd's paralysis, confusion, and weakness.

When first seen in the hospital there were overt signs of a cerebral neoplasm. While the motor signs of left-sided hemiparalysis were interpreted in conjunction with the EEG findings of a right frontal tumor, the marked left-sided ataxia could not be ex-

plained. The x-ray contrast studies permitted the diagnosis of a deep-seated tumor of the anterior midline structures which upon partial removal proved to be an astrocytoma. It is noteworthy that after this operation the ataxia has cleared completely, while the mental symptoms remained essentially unchanged.

### DISCUSSION OF CLINICAL OBSERVATIONS

Although individually different, these four cases exhibit a marked degree of overall uniformity. After a period of progressive emotional instability extending over months or years, general signs of intracranial neoplasia in the form of dizziness, weakness, incoordination, memory impairment and papilledema become manifest. There was also agreement among the cases with respect to the EEG findings, consisting of a generalized slowing to 6–9 cps and focal slowing in either of the anterior quadrants to 2–4 cps accompanied by markedly decreased voltage. This later phase lasted only several weeks.

At autopsy, gliomas of the spongioblastic or astrocytic type originating in the septum pellucidum and infiltrating the adjacent structures where found in each instance.

These observations lend support to Ransom's original hypothesis which related tumors of the anterior midline structures causally to abnormal affective behavior (14). Similar cases were reported subsequently by Wolf (20), by Riskaer (15), and by Haberland (6). It is interesting to note that Jaeger and Bannwarth (9) also observed abnormal affective behavior in an instance of a septum pellucidum cyst.

Ransom's hypothesis was based entirely upon an observed empirical relationship, since at that time nearly nothing was known concerning the biology of cerebral neoplasms and the function of the structures in which he had located the tumor. His observations and conclusions were not only valid, but were made without benefit of the rationale which was provided by neurophysiological and behavioral facts to be discovered much later.

### PATHOLOGICAL CONSIDERATIONS

Ransom (14) pointed out that increasing stupor was observed only in fast-growing neoplasms. This conclusion appears well founded since the typical glioblastoma multiforme of the genu of the corpus callosum invariably grows rapidly into the white matter of both frontal lobes in a butterfly fashion. On the other hand it but rarely involves the underlying structures, namely fornix, septum pellucidum and anterior thalamus.

In contrast, slow-growing tumors were considered by Ransom as those leading to emotional instability. Again there is excellent correlation because neoplasms of the spetum pellucidum are predominately astrocytic or spongioblastic gliomas (8). For a long time these tumors remain restricted to their site of origin, while later they may infiltrate along white fiber tracts. The structures most regularly affected by tumors of the septum pellucidum are fornix, anterior thalamus, corpus callosum, and subcallosal bundle. By extended infiltration the hippocampus, pyriform cortex and pars optica of the hypothalamus may also become involved.

These are among the structures which Papez (12) in his now classical paper proposed as the morphologic substratum of emotion.

### PHYSIOLOGICAL CONSIDERATIONS

Subsequent to Papez' hypothesis (12) and the discoveries of Kluever and Bucy (11), the structures implicated in the mechanism of emotion became subject to intensive study, and have been reviewed in detail by Brady (3).

The question most pertinent to this report is: What psychological changes can be expected from lesions and tumors involving the septum pellucidum and adjacent structures? Unfortunately there is no direct

or final answer to this question as yet, although experimental studies have provided a foundation and framework for speculation. Very little is known in regard to man. That bilateral fornicotomy (performed for epilepsy) results in an acute Korsakoff-like syndrome was shown by Hassler and Riechert (7), and Sprofkin and Sciarra (17) report similar psychological symptoms in a case of glioma of the septum pellucidum and fornix. Interruption of the fornix bundles could conceivably explain the confusional states and the confabulations encountered in our cases. However, one should not lose sight of the fact that in a tumor of this location other structures are also involved.

According to Rothfield and Harmon (16), bilateral fornicotomy in the cat results in a striking decrease in the threshold for rage if preceded by neocortical ablation. Studies by Brady and Nauta (4), and by King (10) on the rat showed that electrolytic lesions of the septal area lead to hyperemotionality as evidenced by extreme reactivity to stimuli and outbursts of attack and flight reactions. In such experiments the precommissural fornix system, in addition to the septal nuclei, is destroyed. Especially noteworthy in these animals is a highly exaggerated startle response to auditory and tactile stimuli. It is interesting to note, in this connection, the great sensitivity to startle in our Cases No's. 3 and 4, although such behavior was not observed in the other two cases.

Although experimental hippocampal lesions have at times failed to produce overt emotional changes, and in other instances have resulted in either decrease or increase in affectivity (5, 13, 18), the fact that both clinical and experimental injuries to the fornix bundle (16) result in hyperemotionality suggests that the hippocampal-fornix system may act as a pathway for inhibiting influences from rhinencephalon to hypothalamus. It is clear that such generalizations must be made with considerable caution and respect for differences in species and stimulus situations.

Whenever an attempt is made to integrate clinical and experimental material of the type presented here the problem of whether tissue changes and consequent alterations in emotional behavior following surgical ablation and electrolytic lesions are truly comparable to those observed as a result of tumor manifests itself. As an initial approach to this problem, five rats were subjected to tumor transplantation by the present investigators. Approximately .001 ml. of a rat sarcoma cell suspension was injected through a 20 gauge needle inserted with a stereotaxic instrument into the septal area.[4] As a control for the effects of an irritative foreign substance in the brain, five additional rats were injected with the same amount of a liver cell suspension. Unfortunately only one tumor transplant was successful, but this produced the only rat in the series with a definite and significant hyperemotionality as measured by a rating scale technique previously reported by King (10). This animal became vicious, fearful, and unmanageable, and its behavior was similar in all observable respects to the increase in affectivity seen following electrolytic lesion of the septal area. No other animal, in either the tumor-injected or liver-injected groups, showed any behavioral changes. The hyperemotionality appeared a few days following transplantation and the rat reverted gradually to a normal emotional level after 14 days. The animal did not show signs of disease until sacrificed four weeks later. Post mortem revealed that the tumor became arrested after having reached a size of 2 x 4 x 3 mm. and was located in the anterior septum, extending upward through the corpus callosum and interhemispheric fissure.

The growth period of subcutaneous trans-

[4] The sarcoma (osteogenic fibrosarcoma 344) inoculated in M/520 rats was kindly placed at our disposal by Dr. C. Snell, Section of Pathology, National Institutes of Health, Bethesda, Maryland.

FIG. 4. Rat brain, frontal section at the level of head of caudate. Van Gieson, 8X. Arrested sarcoma involving rostral and anterior septum and overlying cingulate cortex.

plants of the same tumor in other animals was from 10 to 14 days. It thus appears that hyperemotionality in the animal with the transplant correlated with the growth period of the tumor, rather than with the presence of the arrested neoplasm proper.

Although one hesitates to draw conclusions from a single instance, it seems worthwhile to note that certain behavioral changes resulting from intracranial tumors may be more closely associated with the dynamics of the expansion of the neoplasm than merely with its space-occupying effect.

## CONCLUSIONS

The hypothesis correlating neoplasia affecting the septum pellucidum and the adjacent structures with abnormal affective behavior has been strengthened by further clinical observations. In addition, the modern concepts of the mechanism of emotion both from an anatomical and a physiological point of view seem to support this hypothesis. In our own study we attempted to explore the problem of the degree to which a neoplasm will produce behavioral changes similar to those which follow electrolytic lesions. Although the technique was only partially successful, it was found that tumor and experimental lesions produced strikingly similar behavioral results. In addition, the notion that mechanisms associated with expansion of the tumor are sufficient to interfere with normal functioning of the structures involved was given support. It appears reasonable to conclude that a clinical syndrome of hyperemotionality may be associated with tumors of the anterior midline structures, more specifically of the septum pellucidum and fornix.

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# THE RE-ENACTMENT OF THE MARRIAGE NEUROSIS IN GROUP PSYCHOTHERAPY

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In previous papers (1, 2) we have described two instances of the marriage neurosis, its relation to therapy, and two procedures for its treatment. In this paper we will describe a third variation of the marriage neurosis leading to a stalemate in the treatment, and a technical device to overcome it. The third procedure temporarily introduces the patient's marriage partner into her therapy group where the marriage neurosis is re-enacted, interpreted, and resolved to the extent that it can no longer function as a resistance to the patient's therapy. Finally, we will compare the methods for treatment of the marriage neurosis that involve the use of group therapy, and clarify their indications.

## CASE HISTORY

Mrs. V. is an art teacher in high school. She is 30, and married to a 40 year old widower with two small children by a previous marriage. She came to treatment because of obsessive-compulsive thoughts and such fears as that she might commit suicide by drowning, that she might stab her mother, strike another person, run nude out of the house or "go crazy". She was sexually frigid. The patient has been coming once a week to individual treatment, and once a week to group therapy for four years.

Mrs. V. has an older brother and sister and a brother six years younger. Her father was a commercial artist. She remembers him sitting around the house and her mother "waiting on him hand and foot, and during meals serving him the most and best of everything." The mother over-indulged the patient who "whined" for her to dress her and do favors for her.

The birth of her younger brother activated strong feelings of rivalry and envy. She did not want to grow up and she wanted to be a boy. She pulled on her nose to make it grow; while masturbating she held a small piece of metal next to her genitals and pretended it was a penis. She took over the care of her baby brother and played "mother" to him for many years.

Her father was friendly and participated in her interests. The patient was disappointed that her parents would never leave the house. Her father was a puritan in his thinking, and she accepted his moral concepts. As a young woman she did not want to marry, but later changed her mind because of the thought of coming home to an empty house. She believed the only happiness in marriage was through the children and that men only wanted to be babied.

Mrs. V's father died during her second year of college. She felt a great loss and began attending church, believing that in church she could be close to her father. Her mother turned to her for consolation, saying the daughter was all she had left and they should spend their lives together. The patient took her father's place in the home and resumed the mother-child relationship.

Eighteen months after her father's death, her mother remarried. The patient's stepfather was even more passive than her father had been and again her mother waited on him hand and foot. Her mother's second marriage repeated the earlier situation where her younger brother and her father interfered with her infantile relationship to her mother.

The patient left home and tried to recapture the mother-child position by enter-

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ing a homosexual relationship. She enjoyed most the mutual breast sucking. Her friend would not attempt to find employment and the patient supported her. She began visiting her step-father and mother, and during these visits her neurotic symptoms began. She soon returned home.

Mrs. V's symptoms were activated by her mother's second marriage. The fear of drowning herself represents the wish for union with the mother and the fear of the loss of ego-identity, "going crazy" was pictured as falling to the ground, thrashing about, and yelling, which she had done as a child. Thoughts of striking a person were fantasies of hitting men on the nose or kicking them in the genitals. The patient thought her mother re-married because of sexual needs, just as she unconsciously believed her mother had preferred her baby brother because he possessed the penis she lacked.

The patient could not tolerate living with her family, but was afraid to leave because of the fear she could not control her homosexual wishes. She became anxious to find a husband and soon became engaged to be married. She started treatment three weeks before her wedding.

### THE MARRIAGE NEUROSIS

The patient's wish to find gratification, in the marriage, of dependent, possessive longings for her mother was shown in a day dream. In the dream, her husband took her, on their honeymoon, to an isolated cabin in the snow covered mountains, where they only sat in arm chairs in front of the fire holding hands.

The day dream symbolized the wish to create a marriage relationship where she played the roles of the infant, her father, brother, and step-father. Her husband played the role of her mother. She lost interest in her outside activities and discontinued them. She induced her husband to give up his outside activities and stay at home with her. She took little interest in the cooking or the house work and Mr. V. began to take over these tasks. She tried to quit her job. She discontinued making suggestions to her husband and began to leave decisions up to him. She no longer initiated conversation and became sexually frigid.

### COURSE OF PSYCHOTHERAPY

The patient and her husband regressed in their marriage neurosis to the level of an oral dependent, mother-child relationship. Although the therapist was aware of this development, the treatment became ineffectual due to the degree of neurotic gratification. Interpretations had little influence. It was just possible to prevent her from quitting her job by pointing out that if she did not work she would be financially unable to continue the treatment.

In her individual sessions Mrs. V. soon developed an oral dependent transference neurosis that could not be resolved by interpretation. She behaved in treatment like an infant; as she had behaved toward her mother until she was nine years old. She pretended helplessness, expecting the therapist to answer her questions and give directions. She expected him to fulfill all her dependent needs, as her mother had done. She made little therapeutic effort and either ignored interpretations, rejected them, or responded to them with a question. She obtained gratification by playing the role of the child and was able to maintain the unconscious fantasy that the therapist would play the role of her mother.

The patient began to develop a similar gratifying transference neurosis when taken into group psychotherapy. She was adept at playing the role of the helpless, hungry infant disguised as the co-operative patient who needed help. The group members answered her questions, gave suggestions, and discussed her problems. She could arouse the group's maternal feelings in spite of the therapist's repeated interpretation to the group of the mutual acting-out of the

mother-child relationship. When the group would not "mother" her for several consecutive sessions, she sat and said nothing. Mrs. V. had succeeded in recreating the original mother-child relationship in her transference neurosis in both individual and group sessions as well as in her marriage neurosis, without giving the therapist a chance to utilize and analyze this transference entrenchment efficiently.

The group members gained some insight into their relation to Mrs. V. They, as well as the therapist, interpreted her coldness, lack of interest in others, insincerity, and lack of responsibility. The pretended helplessness and weak therapeutic effort was interpreted, but she responded as if she had no conscience and made no use of the interpretations. For approximately a year the therapeutic outlook seemed hopeless. Finally and as a last resort, the patient's husband was introduced into the group. He attended seven consecutive sessions and two months later an additional five. During these sessions Mrs. V. and her husband enacted the marriage neurosis and it was effectively interpreted by the group members and the therapist. While her husband was present in her group she gained enough insight into the marriage neurosis as a defense against her therapy that her treatment progressed satisfactorily.

In the beginning of their joint group psychotherapy Mr. and Mrs. V. barely spoke to each other. One of the group members remarked at the "cold distance between them." They both said they felt this and that it was true outside the group as well. Mr. V. admitted discomfort in the marriage because of it. Later Mrs. V. said they had sexual problems and repeated the familiar statements of her good intentions, to the effect that she wanted to solve them and was trying to do so. Her husband responded with a similar sentimental attitude, saying he believed that he and his wife loved each other and that their problems would be worked out through her treatment. In response to the group's questions Mr. V. indicated that his beliefs were influenced by his wife's attitude. A mutual reinforcement of their denial of reality became apparent. Their marriage was in effect a mutual defense pact.

They were the only couple in the group. Because of the sharing and integration of defenses the group treated the couple as one unit in the sense that interpretations were directed at the two together. The group interpreted the behavior and attitudes which were both defenses against the marriage neurosis and resistances to the treatment. In confirmation of the interpretations, Mr. and Mrs. V., acting as one unit, revealed the structure of the marriage neurosis itself.

The couple began talking to each other in the group, but with a polite lack of frankness.This resistive attitude was noted. Mrs. V. again brought up their sexual problem. She felt guilty because she could not have an orgasm. Her husband gallantly assumed the blame, saying he probably did not have enough staying power. The group suspected his masochistic attitude with Mrs. V. and he divulged that he had been fully potent with his first wife. Mrs. V. then disclosed that she had no interest in sex with her husband. This was a surprise to him and he appeared shocked and hurt.

The lack of affection between them was then discussed. Mrs. V. felt guilty because her husband compared her to his first wife, who was an affectionate person. By now Mr. V. was becoming disturbed by his insight into the marriage. There was sadness in his voice as he verbalized his unhappiness. He compared the patient to his first wife, who was affectionate, companionable, and good. He said the present Mrs. V. was unaffectionate, uncommunicative, a disorderly housekeeper, lazy and irresponsible.

At this outpouring Mrs. V. became disturbed. It was the first time the group had seen her upset. She sat up stiffly, stared blankly ahead and looked as if she would

break into tears. She could not admit her feelings about the situation until five months later. She felt hurt and depressed and went off by herself to cry. She began to think seriously of her situation and realized she would have to work in her treatment.

There were two further developments. After Mr. V. revealed his wife's role, the group brought out his role in the marriage as enacted with his wife in the group. His submissiveness was held up to him and he gave confirmatory associations which pictured his lifelong passive resistive relationship with his mother. He started to resume his outside interests and social life, turned the household chores back to his wife and took a firmer attitude toward her.

The therapist actively interpreted the influence of the marriage neurosis on the transference neurosis and showed how they were related. This was to confirm what had been started by the group.

The purpose for which Mr. V. attended the group sessions had been accomplished and he was dismissed. The mutual, interlocking defenses of the marriage neurosis were enacted before the group and interpreted. Mr. V. played the role of the indulgent, all forgiving mother who can see only good in the child and has a plentiful supply of rationalizations to justify its behavior. His wife played the helpless child and accepted the feeding provided so abundantly by her husband in the group. This enactment of the structure of the marriage relationship was effectively interpreted and related to the structure of the transference neurosis. In this way the marriage neurosis was rendered ineffective as a resistance to therapy. After Mr. V. left the group, his wife continued the process of working through the transference neurosis and her oral dependent, childhood relationship to her mother.

The question could be raised as to why the usual interpretive technique of psychotherapy or group psychotherapy was not sufficient to make any impression on the patient and why the technique described here turned out to be more effective. The following reasons are offered. There was a lack of gratification in the new situation which upset the neurotic equilibrium established between the husband and his wife's neurosis. The second effective dynamic change was the shift in the transference relationship to a triangular relationship—involving the first wife—the moment the husband appeared within the group. The third factor concerned the inefficiency of the defenses within the new setting: the marriage neurosis could be observed in full bloom when the husband appeared and only then could it be effectively experienced and effectively interpreted by the analyst.

Two years after the therapeutic episode described here, the patient's symptoms had improved considerably. The intensity of her phobic fears had diminished and she became more effective in her work at home. She became active and self sufficient, as she had been before her marriage. She assumed her responsibility as a housewife, and took care of her two step-children. Most important, she became a companion to her husband rather than playing the role of his child. Together, and separately, they resumed their outside interests. Her frigidity changed in that she developed a growing interest in sexuality and began to feel a definite enjoyment in sex. A genital maturity was in sight, even if it had not yet been reached. The patient is still in therapy where she participates more actively than before.

## DYNAMICS

The dynamics of the patient's neurosis as transferred to her marriage and her treatment are the same. Mrs. V. was orally fixated throughout infancy and childhood. The birth of her younger brother was traumatic, and resulted in a further fixation on the oral-dependent position. Later she established some relationship with her father.

After his death she lived alone with her mother and regained the oral-dependent position. When her mother remarried, the stepfather replaced her. The original trauma of the birth of her younger brother was repeated. She reacted by seeking oral gratification in an overt homosexual relationship. She developed her symtoms when she returned home and witnessed her step-father playing the role she herself desired. In her husband, the patient found the final opportunity to recapture the oral dependent position. She married Mr. V. in flight from over homosexuality and in her marriage neurosis recreated the original mother-child relationship. She was sexually frigid because she expected only to receive in the relationship. The patient succeeded in entrenching herself in that kind of transference neurosis which made verbal interpretation ineffective. The setting of individual and group psychotherapy gave her so much oral gratification of her dependency needs that she settled down in a satisfied state of passive resistance.

The entrenchment was loosened by bringing her husband into her group. The patient reacted with shocked surprise to statements made by her husband and by the group and the therapist in her husband's presence. These statements were no different in content than interpretations given to her many times previously in the group and in individual sessions. Mrs. V's super-ego functions had been assigned to her husband. Interpretations had been made to her, so to speak, in the apparent absence of her super-ego. When Mr. V. joined the group the same interpretations were effective because they were offered in the presence of her super-ego. Because she regressed in the marriage relationship she was able to divide the internalized mother figure into the good and the bad. The good mother was projected onto her husband, the bad onto the therapist and the group. Only the good mother represented functions of the super-ego. When Mr. V., in the group, appeared to take sides with the therapist and the group, his wife could no longer maintain the division of the mother figure. As the marriage neurosis was effectively interpreted there was a reincorporation of the super-ego and the presence of the patient's husband was no longer necessary for interpretations to be effective.

## CONCLUSIONS

In a previous communication (1) we showed, with a clinical illustration, how the marriage neurosis can stalemate treatment. In that example the primary patient played the role of the nursing infant and his wife the feeding mother. Because he obtained excessive oral gratification in his marriage he was able to maintain a division of the internalized mother figure. In the marriage neurosis his wife was the good mother; in his transference neurosis the therapist was the bad mother for whom the patient would make no therapeutic effort. When the wife, as a result of her therapy, deprived him of many of his oral gratifications he could no longer maintain the division of the mother figure, and turned to the therapist as a father figure to be pleased. Only then did the patient's therapy become effective. When both marriage partners are treated concurrently, but separately by the same therapist, their progress can be integrated. When the couple is in treatment with the same, rather than different therapists the interpretation of their joint interlocking defenses can be more effectively timed. This is true although the two hold frequent consultations.

In a second paper dealing with this problem, we presented a patient who was acting out his hostility to his mother in his marriage, and was able to defeat the purpose of his therapy by acting out an ambivalent, homosexual attachment to his father in the transference neurosis. When it became clear that the marriage neurosis prevented the treatment from being effective, the patient's wife was introduced into his therapy

group. She did not offer to participate as a patient and was not encouraged to do so. Her presence alone reactivated the oedipal conflict and altered the transference neurosis because the original triangular situation was recreated. The therapist, who in the eyes of the patient had been the bad father to be defeated, became the good father to be pleased in competition with the mother, in the person of the patient's wife. A workable transference was established and interpretation became effective. When a certain amount of insight was gained by the patient, the marriage neurosis was no longer used as a defense against the treatment.

The therapeutic impasse described in the present paper was also a result of excessive, neurotic gratification in the marriage neurosis. The difficulty was again resolved by bringing the patient's marriage partner into her therapy group, but in a different way. The patient had established the same mother-child relationship in both the marriage neurosis and the transference neurosis. Her husband was temporarily introduced into her therapy group and encouraged to participate as a patient. The couple enacted the marriage neurosis; the therapist and the group interpreted the mutual interlocking defenses against insight into the marriage relationship. When the patient gained insight into her marriage neurosis and related it to her transference neurosis, the marriage neurosis lost its effectiveness as a defense against the treatment.

When these methods of bringing the marriage partner temporarily into the patient's group are used, an important consideration is whether or not the spouse is to participate as a patient or a visitor. There is a tendency for the right method to develop spontaneously; the therapist may be called upon merely to guide the process. The spouse should not be involved as a patient, if in the beginning the presence of the marriage partner stimulates the patient to productive therapeutic activity. When the presence of the marriage partner does not alter the primary patient's transference neurosis the therapist may allow the mate to become involved as a patient and in this situation the marriage neurosis will be re-enacted. If, as in the present case, the dynamics of the transference neurosis and the marriage neurosis are the same it will probably be necessary for the marriage neurosis to be re-enacted and interpreted in the group setting. When the therapist is a different parent figure to the primary patient than the marriage partner, or represents a different aspect of the same parent figure, it may be necessary for the therapist to prevent the mate becoming involved as a patient.

The timing of this therapeutic strategem is important. The patient's spouse should be introduced into the group after the transference neurosis has been established; after it is apparent that there is a therapeutic impasse, and that the block is due to the influence of the marriage neurosis. This procedure is not recommended for other treatment difficulties. Neither is it offered as a substitute for the working through of the transference neurosis. It is used to make effective interpretation of the transference neurosis possible. We have seen that this is a powerful therapeutic tool aimed at the patient's defenses. It is not recommended where defenses are needed against a schizophrenic break-through or a depression.

The marriage partner is kept in the group only long enough to render the marriage neurosis ineffective as a defense against the treatment of the patient. This may take a few sessions or many. Should the procedure be unnecessary or should the marriage partner be kept in the group after the purpose has been accomplished, his presence may be used by the primary patient as a resistance. If the original resistance re-occurs, because the defenses were not sufficiently interpreted, the patient's mate may be brought back to the group as before.

The authors believe the temporary introduction of the marriage partner into the patient's therapy group, in certain instances, can succeed where other treatment methods would fail.

We have attempted to illustrate with case material the indications for this new variation of group psychotherapy and we have tried to describe its dynamics. We hope to determine with further experience in clinical observation in which cases a permanent, simultaneous and concurrent psychotherapy or group psychotherapy of married couples is feasible. Critical to this strategem, of course, is the professional orientation of the group therapist, his countertransference and scientifice orientation to his work.

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# PSYCHOTHERAPY OF THE ADOLESCENT: A COMPARISON WITH PSYCHOTHERAPY OF THE ADULT

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Psychotherapy of the adolescent has received some attention in the literature (1–6). However, there is a need to clarify the actual therapeutic techniques used with adolescents and to demonstrate how these techniques differ from those used with adults. This paper is an effort to approach the problem in a systematic way, in order to clarify impressions and present factual material that can serve as a basis for discussion and further elucidation. In order to facilitate understanding, dynamically oriented psychotherapy of the psychoneurotic adult is compared with psychotherapy of the adolescent. This creates a degree of artificiality on both sides that can be held in perspective if it is kept in mind that any given case may require many exceptions.

The different therapeutic approach with adolescents is based on the theory that the adolescent's emotional structure differs essentially from the adult in ways presented in Table 1.

For the purpose of understanding, treatment is divided into three phases.

1. *Initial Phase:* from the first contact to the development of a therapeutic relationship.

2. *Relationship Phase:* from the establishment of a relationship to the termination of treatment.

3. *Termination Phase:* termination of psychotherapy..

The techniques used with adolescents and how they differ from those used with adults are presented for each of the three phases.

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## INITIAL PHASE

With the adult, the burden of establishing a therapeutic relationship is on the patient and the psychiatrist aids by reflecting the patient's distortions. For several reasons, the burden of establishing a therapeutic relationship with adolescents rests with the psychiatrist. The patient is separated from the world of adults and he sees all adults as prototypes of his parents. In addition, he has often been traumatized by his parents, which makes him more defensive. He may also have been coerced into seeing the psychiatrist. These factors affect his therapeutic relationship. He may approach the interview with considerable resistance, which may be manifested by resentment, withdrawal, negativism or suspiciousness. The degree to which the parents have distorted reality in their handling of the patient and the degree of the patient's illness will determine the efforts that have to be made by the therapist to establish a relationship. The therapist's initial efforts must be directed towards dissociating his behavior from that of the patient's parents. This is aided by seeing the patient first and obtaining his view of the problem. This also respects the patient's strivings for independence. However, it is also most important to see the parents. If the parents' personality is pathological, the relationship of this pathology to the patient's illness must be determined. Where there seems to be a direct interlocking relationship, it would be difficult to help the patient without getting help for the parent. The parents' pathological behavior must be seen in the same light as a symptom, *i.e.*, that it meets an emotional need, and may have deep roots.

TABLE 1

*Theoretical Differences in Personality Structure*

| Adult | Adolescent |
|---|---|
| 1. Unconscious drives relatively repressed and held in control by defenses. | 1. Unconscious drives reinforced, poorly repressed, under precarious control of defenses. |
| 2. Defenses relatively strong. | 2. Defenses relatively weak. |
| 3. Has achieved a working set of values or standards which represent a compromise between childhood superego demands and later environmental influences. | 3. Is actively trying to achieve a set of values by resolving the conflict between childhood superego demands and later environmental influences. |
| 4. Able to function at a job and usually living away from the parents. | 4. Functioning in school often decreased, and therefore not supportive. Living with and under control of parents. |
| 5. Has made some working compromise with emancipatory strivings and sexual drives. | 5. Actively, intensely trying to resolve emancipatory and sexual conflicts. |

*Example of Interlocking Psychopathology:*

A 17 year old, intelligent, high school senior was brought to the clinic after being arrested as a peeping Tom. An interview with the mother revealed that she and the patient live alone in an apartment. She often walks nude in the apartment, and often leaves the shower door open.

The doctor has many tools for establishing a relationship with the patient. First, he must tolerate the patient's defensiveness without this evoking his own defenses in turn. This encourages the patient to reveal his need for help. He should concentrate on the patient's immediate feelings and wherever possible clarify them. The exact technique depends on many factors, and the amount of time necessary to establish a relationship may vary from one interview to a period of six months or more. Two examples are given: the first is an example of establishing a relationship in one or two interviews with a neurotic patient through direct interpretation of her behavior; the second is an example of the need for months of slow, painstaking effort with a schizophrenic patient.

*Examples of the Initial Phase of Treatment:*

A 17 year old, wealthy, attractive, debutante was seen at the request of her physician for being rebellious at home, being expelled from school and abruptly planning a marriage. As the psychiatrist entered the room, the patient took the offensive, attempting to place the interview on a social basis, asking personal questions of the doctor, making provocative comments regarding his reactions, and in general, trying to control the interview. During this time, the psychiatrist was trying to respond appropriately to the patient and at the same time to obtain a quick evaluation of the patient. As soon as he decided that the patient was probably neurotic, and not schizophrenic, he interpreted to the patient her aggressive, competitive behavior as a sign of anxiety. This led to an obvious relaxation in the patient's anxiety, a change in the whole tone of the interview, and a discussion of her use of this technique with everyone as a defense, and finally, its use with her father. This in turn led directly to a discussion of her disappointment in her father, and her anger at him and her mother for their divorce.

At the opposite extreme is the following patient, where it took many months and a variety of therapeutic techniques:

A 14½ year old schizophrenic girl was seen for poor marks, shyness and depression. From the initial interview, the patient was restless, anxious, tense and silent. The only thing she volunteered was her resentment at her mother's prying. It was

made clear that the doctor was not here to pry and that she did not have to talk if she did not want to. The patient expressed a desire to talk but had difficulty in starting. She was an avid reader and attempts to establish contact were made through discussion of the various books she was reading. For example, a discussion of *The Brothers Karamazov* led to a discussion of sensuality and her fear of sensuality. A discussion of *The Man In the Grey Flannel Suit* led to the expression of her feelings that the mother was driving, made all the decisions, ran everything and the father needed pushing by the mother. Next, the doctor accepted the patient's difficulty in talking and suggested that she pick a topic. This led to a discussion of her anxiety about her mother and sister's fighting. Somewhat later, it was noticed that the patient was sewing in the waiting room. When asked about her interests, she said she also enjoyed painting. When asked why she would not bring a painting in, her feeling that they were not good enough was expressed. This led to a discussion of her need to maintain an appearance and put on a show in the interviews. At another time, the patient questioned the doctor about herself, but parried any of his attempts to get her to express herself. When this was brought up with the patient, she mentioned her fear about talking about certain things which she didn't want the doctor to know. Several interviews later, with considerable difficulty, she expressed feelings of guilt and anxiety about an affair that had been in progress with a school teacher twice her age.

### RELATIONSHIP PHASE

With the adult, as the relationship is established, the psychiatrist continues to reflect rather than respond to the patient's emotions. He encourages the expression and analysis of instinctual wishes and uses what may be called "open" questions and interpretations designed to explore the underlying conflicts. An open question consists of asking the patient a general "why" with regard to his behavior, *i.e.*, "Why do you feel that way?" This results in the relaxation of repression and the production of anxiety. The patient is expected to locate and identify the emotions, to handle impulses that arise, and also to manage the attendant environmental problems. Investigation and understanding of the fantasy and sexual life is stressed, and the psychiatrist may foster a transference relationship through relating emotional reactions which arise to the therapist to their unconscious and historical context. In this transference relationship, the patient repeats his neurotic problems.

The psychiatric function with the adolescent is quite different. Control rather than understanding is stressed and fantasy and sexual life are not probed unless the patient initiates it. The psychiatrist attempts to respond to, rather than reflect, the patient's emotions. He allies himself with the ego and uses "closed" questions focused on specific areas to reinforce repression and relieve anxiety.

A closed question consists of asking the patient a specific question. This encourages the consideration of the specific areas which are within the patient's control rather than opening up all areas which may lead to the impulses that are not within control, *i.e.*, "Do you feel that way because you are disappointed?" The therapist does not expect the patient to locate and identify emotions but rather attempts to anticipate and clarify the patient's emotional reactions for him, pointing out the distortions. He minimizes the historical aspect of the relationship by focusing treatment on the contemporary level, clarifying present reactions, pointing out distortions, and responding in such a way as to give the patient a corrective emotional experience. Though the transference feelings are not stressed, there is no doubt that identification with the therapist plays a strong part

in the therapeutic effect. Following are examples of the factors stressed above.

*Example of Clarifying Immediate Feelings:*

A 15 year old girl, in the eleventh grade, presented a history of depression and suicidal preoccupation in a setting of conflict with her mother. At the first interview, the doctor was fifteen minutes late and apologized. The patient immediately stated that she couldn't make the next appointment as it was inconvenient, that the psychiatrist couldn't keep mother from being angry at her. She then went on to express how she needs a boyfriend to be close to, to understand her; that older people don't know about emotional problems, and they only give you biased advice. Next, she expressed her need to be self sufficient, and to learn from her mistakes.

*Therapist's Comment:*

To an adult: "I wonder if these feelings might be related to my being late." To an adolescent: "It seems to me that the feelings you're expressing are related to what happened this morning. You felt the need to talk to me, made an effort to be here on time and then you felt disappointed and angry when I was late, expressing it by withdrawing into yourself, acting independently, and not coming to the next interview. I wonder if you don't feel my being late means I'm not really interested." This incident was then developed and related to the relationship with her mother.

*Example of Therapeutic or Corrective Emotional Responses:*

A 17 year old girl, a high school senior, had a history of depression, social withdrawal, and difficulty in school. In the interview, the patient recounts feelings of inadequacy, parental rejection, and how she keeps her accomplishments to herself as parents rarely react. In this situation, the psychiatrist kept in mind that the patient would probably make indirect, tentative moves for approval, and these were encouraged and responded to. In contrast, in the adult, the patient's feelings regarding the parents' lack of reaction would be analyzed.

*Example of the Approach to Adolescent Pathology:*

A 17 year old boy, a high school senior, had a history of lying, keeping late hours, being careless with money, and decreasing efficiency in school in the setting of a conflict with his father. Onset of symptoms coincided with remarriage of the father to a girl in her late twenties. Prior to the marriage, his father (probably a psychopath) had indulged the patient, but after marriage, under his wife's influence, the father was arbitarily punitive and restrictive with the patient. The patient was in danger of being expelled from school. In the interviews, the patient expressed feelings of depression, sullenness and withdrawal, followed by impulses to "break rules" at school. It became clear that these feelings were closely related to the father's punitive activities. It was first clarified that the patient's feelings of depression were related to anger at his father, rivalry with the father's wife, and rejection by the father. Several incidents showed that the patient was attempting to provoke the father by breaking the rules. This led to a discussion of the patient's need for the father, his feelings of anger at being rejected, that resulted in acting out which expressed the patient's anger, provoked the father, and got his attention. During the course of these interviews, the patient became aware of his father's pathology and the self-destructive nature of his own behavior. He was able to exert control and eventually brought his grades up to passing and graduated. Therapy was discontinued at this point without going into the deeper dynamic aspects of the patient's problem. In other words, therapy was directed toward clari-

fying the patient's current emotional reactions. In the adult, the patient would develop a transference relationship which would repeat his neurotic problems with his father. The resolution of the transference relationship would then be the effective force in helping the patient.

With adolescents one must be cautious in pursuing unconscious motivation and the meaning of dreams. Explanations of the significance of dreams or unconscious motivation may only serve to intensify the patient's anxiety about his own instincts, and generally result in an increase in resistance. The adult, however, feeling more secure regarding his capacity to control instinctive feelings, is more ready to consider unconscious motivation.

*Example of Adolescent's Response to Therapist's Interest in Unconscious Motivation:*

A 14 year old patient had a history of enuresis and a hysterical psychoneurotic reaction. In the initial interview, the patient was unspontaneous, responding only to the therapist's questions. The therapist responded to this by using the patient's few productions to illustrate and explain the significance of dreams and unconscious motivation. The patient responded by an increase in anxiety, withdrawing further, and becoming more silent. When her silence was dealt with, it was found to be a means of dealing with her fear that talking about emotions will lessen control, that the therapist is trying to prove she is insane by connecting thoughts. Reassurance regarding these aspects and direction of the interview to current feelings led to a lessening in anxiety and furthered therapeutic progress.

In the adult, the therapist can usually rely on the patient's conscious control of impulses, but with the adolescent, this is often not possible. The therapist must carefully judge the strength of the impulse relative to the patient's capacity for control. This presents a particularly acute problem because of the adolescent tendency to act out feelings in the doctor-patient relationship. The adult will often verbalize these feelings, but the adolescent must have it clarified for him. Failure to do this can often result in the interruption of treatment.

*Example of Exploration:*

A 16½ year old girl had a problem of developing a too close attachment with female teachers, and then annoying them by following them around. The patient's behavior improved under treatment, but in the fifth month of treatment with a male therapist, she suddenly announced she was not in love with her therapist, sought out teachers again, was late for interviews and contacted a female social worker at school to see her regularly. It appeared that the psychiatrist had not recognized the development of strong positive feelings on the part of the patient, and the patient was acting out her resentment. Clarification of this situation alleviated it and led to a discussion of her father's constant rejection of the patient's "needs to be cared for."

Another variation from the adult is the psychiatrists' direct intercession in the patient's environment.

*Example of Intercession:*

This 17 year old senior in high school was briefly presented above. After several months in treatment, he was making a real effort and his behavior improved. However, the stepmother was becoming more anxious and the father decided to leave the city with his wife, leaving the patient with a housekeeper. When he also decided to take the patient's dog that the patient bought with his own money, the therapist intervened. Also, when the headmaster was about to expel him, the psychiatrist interceded on his behalf.

TERMINATION PHASE

In the adult, as the patient has worked through his neurotic problem, he gradually

feels freer, with less need for treatment and with treatment finally seen as an extraneous burden to his life. In this phase, the psychiatrist has already allowed the patient to take over the main burden of solving his problem, and he then proceeds to lessen the patient's dependence gradually, cutting down frequency of interviews and finally terminating with the door being left open for future interviews if necessary.

In the adolescent, the termination of treatment should be kept in mind from the beginning. If the relationship phase of treatment has been properly handled, the termination will be a natural result. If the treatment has been directed toward the present, the patient will not have formed too deep an attachment. If the patient's independence and capacity to handle his own life have been encouraged, the patient will be directed towards leading an active life rather than analysis of motivation. As anxiety diminishes, and the patient feels more control, he will be ready for termination. At this point, it is often the psychiatrist who first recognizes the need for termination and he must formulate it to the patient.

*Example:*

A 17 year old girl in her last year of high school complained of anxiety, nausea, and vomiting before every date. After five months in treatment, the patient's symptoms had disappeared, her relationship with boys had improved, she had graduated from school and was working. When the doctor attempted to change the time of the interview to fit her new schedule, the patient seemed to stress the difficulties. When it was formulated that she was ready to stop treatment, she accepted it readily and with obvious relief.

As in the adult, it is important to keep the door open for future interviews. Unlike the adult, after the end of treatment it is sometimes helpful to maintain contact by sending out greeting cards on special occasions, such as a birthday.

## DISCUSSION

The essential dynamic problem of adolescence seems to lead directly to the core

TABLE 2

*Comparison of Therapeutic Techniques Used with Adults and Adolescents*

| Adult | Adolescent |
|---|---|
| 1. Open questions to stir anxiety and relieve repression. | 1. Closed question to relieve anxiety, give support and reinforce repression. |
| 2. Patient locates and identifies emotion himself. | 2. Psychiatrist helps to clarify the emotions for the patient. |
| 3. Understanding is stressed with emphasis on the investigation of the fantasy and sex life. | 3. Control stressed with fantasy and sex life not investigated unless the patient initiates it. |
| 4. Patient is expected to handle environment. | 4. Patient may require help with school or work. |
| 5. Can rely on the patient's conscious control to handle impulses. | 5. The psychiatrist often cannot rely on the patient's control of impulses. He must judge strength of the impulses relative to the patient's capacity for control. |
| 6. Psychiatrist relates emotions to unconscious and historical context and attempts to reflect rather than respond to the patient's emotion. Thereby he fosters a transference relationship where the patient can repeat his neurotic attachments. | 6. Psychiatrist relates emotions to the contemporary scene; points out distortions and responds appropriately to the patient's emotions as the patient needs to have new healthy emotional experiences in addition to undoing the old. Thereby he also minimizes the historical aspect of the transference relationship. |
| 7. Resolution of the transference relationship is the most effective agent in treating the neurotic adult. | 7. Identification with the psychiatrist is often the effective agent in helping the adolescent to manage his problems. |

of the therapeutic problem. The adolescent is caught between rebellion against the old childhood superego demands as personified by his parents and the need to integrate these old demands with a new set of values presented by the social environment. The rebellion complicates the merging of the old childhood and the new environmental influences. The adolescent then turns to figures outside the family. He creates idealized images and through the process of identification with these images, he attempts to resolve the conflict. This occurs whether the patient is in treatment or not. However, in treatment the therapist becomes this idealized image with whom the patient can identify and whom the patient can use to find a new, adult, ordered solution of his conflict. The idealized image of the therapist serves as a bridge between childhood superego demands and the current demands of reality. The patient uses this bridge to free himself from the rebellion against the childhood superego and to direct his energies towards achieving some satisfactory way of meeting the current demands of reality. In this sense, in contradistinction to what occurs with adults, the therapist becomes a realistic figure who plays an active part in the growth process of the patient. It is for this reason that the particular personality of the therapist is often so important to the success of the treatment.

In order to present material which can be used as a basis for comparison and discussion, one has to accept the many handicaps of attempting to specify psychotherapy. However, it is hoped that additional contributions along this line will eventually lead to an organized body of knowledge regarding the psychotherapy of the adolescent and how this differs from the psychotherapy of both children and adults.

SUMMARY

The theoretical differences in the personality structure of the adolescent and the adult are presented.

The difference in therapeutic technique is derived from the difference in personality structure.

Treatment is divided into three phases: inital, relationship, and termination; differences in therapeutic technique are presented with case illustrations for each phase.

The discussion stresses the therapeutic importance of the mechanism of identification in the treatment of the adolescent.

The conclusion lists the differences in personality structure and therapeutic technique.

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# ALCOHOL, CONVULSIONS AND TRANQUILIZERS: A CLINICAL AND ELECTROENCEPHALOGRAPHIC STUDY

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## INTRODUCTION

The occurrence of grand mal seizures in some persons following ingestion of large quantities of alcohol has long been noted. When the convulsions never occur in the absence of alcoholic intake, the condition has been termed "rum fits" or " alcohol epilepsy." It has long been disputed whether this is a disease entity per se or merely a specific tendency towards seizures activated by alcohol and observed in persons with a low convulsive threshold.

The clinical picture of "rum fits" has recently been somewhat obscured because alcoholics hospitalized for acute intoxication with actual or "impending"[2] delirium tremens, usually receive one of the tranquilizers as the principal therapeutic agent. These tranquilizers, especially the phenothiazine derivatives (particularly promazine and chlorpromazine) and reserpine, themselves cause seizures in certain individuals.

Experimental work on the convulsive properties of the tranquilizers to date has consisted of the treatment of a number of acutely disturbed patients with one of these drugs and then observation of the seizure incidence which resulted. The experiments reported in this paper were designed to observe the effects of tranquilizers and alcohol, both alone and in combination, on the clinical state and the electroencephalogram of an alcoholic with "rum fits". The patient reported in this study had also had a seizure following the administration of chlorpromazine for "impending" delirium tremens.

## ALCOHOL AND SEIZURES

The consumption of alcohol lowers the seizure threshold in epileptics. In one series 1254 epileptics were interviewed, and 57 per cent of those who used alcohol to excess experienced an increased seizure frequency (33). Alcohol in large doses is a central nervous system depressant and therefore acts as an anti-convulsant. Thus the mechanism of the seizures which occur following the withdrawal of alcohol is apparently the same as that of convulsions following withdrawal of large doses of other central nervous system depressants such as barbiturates and paraldehyde (27). It has been shown, however, that in moderate concentrations alcohol ingestion does not diminish either cerebral blood flow or oxygen consumption (13).

*Alcohol Epilepsy (rum fits):* Patients with "alcohol epilepsy", unlike epileptics, never have seizures without the use of alcohol (by definition). The earlier literature graphically described the occurrence of these fits on "the day after return from vacation" (France), or "only on Mondays after their return to the hospital . . . never in saloons or on the street" (Germany) (27). The transition of pure alcohol epilepsy into epilepsy with manifestations in alcohol-free periods does not seem to occur.

The characteristics of "rum fits" have been presented in a clinical analysis of 88 patients with this entity (47). In this group

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[2] This term is used clinically to describe the syndrome of apprehension, tremulousness, diaphoresis, weakness and unsteadiness often seen prior to the development of full blown delirium tremens (16).

no seizures occurred at the beginning of a drinking bout (in spree drinkers) but only after several weeks of constant imbibition. These seizures affected alcoholics only after many years of excessive drinking and, in this series, the onset of the fits was in adult life, usually between ages 30 and 60. Of 78 of these patients, in whom the number of seizures could be accurately determined, 32 had single, 44 had multiple, and two had continuous seizures. Almost all were grand mal in type. Whenever an alcoholic patient presented with focal seizures, focal brain disease was discovered. The majority of seizures occurred evenly distributed over a 48 hour period following the final cessation of drinking. Some seizures occurred during periods of alcohol ingestion, and others over 96 hours after the cessation of drinking. The seizures always preceded the development of a delirium. In this series 20 per cent of the patients had previous cerebral trauma as noted in the hospital records, varying from concussion to compound skull fracture. No abnormalities of blood sugar, NPN, $CO_2$, sodium, potassium, chloride, nor of the brain on pathological examination were detected except for abnormal chemistries in dehydrated patients. Likewise, electroencephalograms taken between drinking bouts or shortly after seizures appeared quite normal in these patients.

The incidence of rum fits among alcoholics is hard to determine. The study most often quoted reports an incidence of 12 per cent or 32 out of 266 alcoholics admitted to Boston City Hospital over a 60 day period (47). The rum fits here are defined as "epilepsy (which) complicated the various alcoholic illnesses in 12 per cent of the cases." This, of course, does not state that these patients had seizures only after alcohol ingestion. In another series of 161 alcoholics, the incidence of epilepsy was over 4 per cent (7 patients), with the explanation that "the alcoholism occurred at the same time the neural disorder appeared or later" (9). In a study of 305 patients who were hospitalized for delirium tremens 384 separate times from 1933 to 1940, 29 of the patients (9 per cent) had convulsions (41). There were 32 instances of convulsions among the 384 admissions (8 per cent). Here, however, all patients who had convulsed only during previous alcoholic episodes (but not this episode) were excluded from the study. Of the 29 patients included, two had a family history suggestive of convulsive disorder and another had convulsed prior to the onset of his alcoholism (*i.e.* idiopathic epilepsy rather than rum fits). Ten of the 29 patients had a reliable history of head injury which preceded the onset of the fits from a number of hours to a number of years.

*Experimental Induction of Seizures with Alcohol:* In one study, following abrupt alcohol withdrawal in six patients after chronic administration (48 to 87 days), two convulsed and three others had a frank delirium (25). Only one patient escaped both convulsions and hallucinations. There were no convulsions or delirium while the patients were drinking. The average daily intake was 266 to 489 ml. of 95 per cent alcohol. The patients were hospitalized former morphine addicts off drugs for at least three months. None had a personal or family history of seizures and all had normal pre-experiment electroencephalograms. During the early chronic intoxication phase of the experiment the tracings revealed slowing. At this time the blood alcohol level was elevated and the patients were clinically intoxicated. Electroencephalograms were not as slow during the late chronic intoxication period; however, blood alcohol levels were higher in the late period than in the early one. With withdrawal of alcohol, a normal electroencephalogram was first present and then, between hours 16 and 33 of abstinence, a decreased alpha activity with random bursts of slow waves and spikes was present.

*Electroencephalographic Studies:* The effect of alcohol, on the electroencephalo-

gram has repeatedly been shown to be a diffuse slowing (50). While the behavioral and electroencephalographic effects of alcohol are generally highly correlated, they may be "dissociated" from the level of blood alcohol during the recovery phase following chronic intoxication or following the administration of single doses (37, 50).

Tracings have been made on patients with rum fits in an effort to establish the relationship of this disorder to idiopathic epilepsy (18, 21). In one series of 24 patients who had no seizures before the onset of their heavy drinking, four had abnormal electroencephalograms (21). One of the four was actively hallucinating and three had clouding of consciousness at the time the records were taken. This series was then compared with that of 115 patients with idiopathic epilepsy with average onset of seizures at the same age as that for the other group (age 35). In this latter group, 75 per cent of the patients had an abnormal electroencephalogram (21). This would tend to support the hypothesis that idiopathic epilepsy and rum fits are distinct entities.

On the other hand, a study of 74 "convulsive alcoholics" revealed normal electroencephalograms in over 59 per cent of the patients (18). In this study, when the patients with normal electroencephalograms *plus* known head injury, abnormal glucose metabolism and seizures independent of drinking were excluded, then the incidence of normal electroencephalograms in "convulsive alcoholics" was raised to over 65 per cent. This incidence was compared by the authors to a series in which 54 per cent normal electroencephalograms occurred in 2,430 epileptics who had only grand mal seizures (19). It also was compared to a normal control group of 1000 subjects of whom 85 per cent had normal electroencephalograms (20), and to an "uncomplicated" group of 81 alcoholics, of which over 79 per cent had normal electroencephalograms (18). The authors concluded from this that this disorder is not different from epilepsy (18).

*Summary:* Seizures following, and only following, alcohol ingestion are termed "rum fits" or "alcohol epilepsy." There is controversy as to whether or not this is a separate entity and can be distinguished from idiopathic epilepsy. The seizure mechanism, however, remains obscure in patients with "rum fits." Experimentally, alcohol withdrawal following chronic intoxication produces seizures in non-epileptic patients. The electroencephalographic changes which occur following alcohol ingestion are predominately those of diffuse slowing.

### TRANQUILIZERS AND SEIZURES

*In non-alcoholic patients with no history of epilepsy:* Reports of grand mal seizures in patients receiving tranquilizers continue to appear in the literature. Many of these patients are not alcoholic and have no history of previous convulsions nor demonstrable organic brain disease. With chlorpromazine these seizures are reported to have followed single doses as low as 25 mg. parenterally (3) and ten mgm. orally (22). In one study on schizophrenics, fourteen seizures occurred in eleven patients out of a group of twenty-one receiving up to 4,000 mgm. of chlorpromazine daily (44). The daily dose before seizure occurrence varied from 200 to 2900 mgm., and the number of treatment days up to the time of convulsion varied from three to thirty-six days. Some of these patients, however, had seizures prior to the seizures while on this intensive chlorpromazine regime.

In another series of 800 patients treated with 150 to 800 mgm. of chlorpromazine daily for acute and chronic psychoses, ten patients had epileptic fits which were found to be unrelated to total dosage of the drug, to dosage at the time of seizure, or to duration of treatment (34). Five of these ten patients had never had previous seizures; eight of the ten, however, had

known organic cerebral changes at the time of seizure. On the other hand, three of sixty psychotic patients who convulsed for the first time on 300 to 2,000 mgm. of chlorpromazine daily, remained seizure-free when the dosage of the drug was reduced. Their pre-treatment electroencephalograms were normal (17).

Seizures on promazine in schizophrenic patients without previous convulsive disorder have occurred. In two of these cases, no difficulties had occurred on similar doses (1200 mgm. daily) of chlorpromazine treatment for eight to twelve months duration (4). In another report, seizures for the first time occurred following oral promazine treatment (48). Seizures on combined parenteral-oral reserpine therapy have been reported in two of 37 patients with functional psychoses. Neither had a history of convulsive disorder (28).

The mechanism of these tranquilizer-induced seizures remains obscure. However, it has been shown that intravenous chlorpromazine has no effect on cerebral blood flow or oxygen consumption (13). Likewise promazine has no measurable effect upon total cerebral blood flow or oxygen consumption (10). And in studies on five hypertensives treated with parenteral reserpine, there was no change in cerebral blood flow, glucose or oxygen uptake, or venous oxygen tension (23). Biochemical investigations of the effects of tranquilizers on isolated enzyme systems have not elucidated the seizure mechanism to date (5).

Electroencephalographic studies in non-alcoholic patients with no convulsive history are essentially non-contributory when therapeutic dosages of the tranquilizers are employed. Chlorpromazine produces normal tracings or patterns similar to that of normal sleep (2, 7, 31, 32, 39, 45). Reserpine, tested in hypertensive patients, causes no characteristic electroencephalographic changes (8, 23). A study of eight patients with implanted cortical and subcortical electrodes revealed no distinctive electroencephalographic changes in either the cortical or subcortical regions before or after reserpine and chlorpromazine. The electrodes were chronically implanted in the septal region and on the pia arachnoid in several cortical regions. Six of the eight patients were chronic schizophrenics, one had terminal cancer, and one was an adolescent with acute rheumatoid arthritis (38).

A case has been reported of an electroencephalogram taken two days following ingestion of several handfuls of chlorpromazine pills (25 mgm. each) in a suicide attempt by a 19 year old, non-epileptic female (35). This revealed "a moderate number of diffuse and symmetrical bursts of spike and wave patterns with frequencies of 3–4 per second." A second electroencephalogram, taken twelve days later, revealed no spike and wave activity nor any other abnormality. Another case is reported of suicidal ingestion of 50–100 chlorpromazine tablets, 100 mgm. each, by an 18 year old girl. The patient went to sleep two hours following this ingestion and by the 12th hour could not be roused; her deep tendon reflexes and plantar responses were then absent. From the fifteenth to the eighteenth hours, three convulsions occurred. An electroencephalogram taken one-half hour following the first convulsion revealed "paroxysms of spike and slow waves with a duration of 1–2 seconds on a background pattern usually seen during the transition from drowziness to light sleep." Though this patient had no history of previous seizures, a "routine" electroencephalogram performed one month earlier had revealed "anterior temporal and middle temporal random spikes bilaterally." (43)

*In non-alcoholic epileptics:* There is some controversy concerning the effect of chlorpromazine on convulsive seizures in epileptics. One case of "cerebral dysrhythmia" has been reported where the electroencephalogram showed improvement on chlorpromazine (40). Both the clinical and

electroencephalographic signs of grand mal epilepsy disappeared in another patient while being treated with a 100 mgm. daily dose of chlorpromazine over a two-year period (6). On the other hand, intravenous chlorpromazine was administered in therapeutic doses to twenty epileptics and eighteen of them developed an increase in paroxysmal cerebral activity, although no seizures were produced (11). There is evidence that overt and latent epileptics show either an increase in frequency or an appearance of seizures within a week of starting drug therapy (42). Some authors state that the drug has no effect at all on convulsive seizures (7).

The effect of promazine on the cerebral electrical activity of twenty-one subjects with a history of convulsive disorder was recorded in an electroencephalographic study with tracings before and up to two hours after promazine administration (12). None of these patients convulsed, seven had sleep spindles on their electroencephalograms, all became more relaxed, and in only one patient was there any activation. Four other patients with a seizure history were given an activating oral dose of metrazol and electroencephalograms were taken before and after oral promazine administration. There were no seizures nor changes in the tracings (12).

Reserpine was given to 220 epileptics in a study where 397 electroencephalograms were taken without demonstration of any specific pattern that could be ascribed to the drug (30). In another experiment, 30 male epileptics on anti-convulsants were divided into two groups, matched for seizure frequency. One group was given daily oral reserpine and the other a placebo for 45 days. An analysis of the results revealed a statistically significant effect of the tranquilizer in decreasing the number of seizures (29). Reserpine has also caused a cessation of seizures in three patients in status epilepticus when given intramuscularly (29).

*In alcoholics:* One study has been reported where over 3,000 acutely disturbed patients were treated with chlorpromazine or promazine and observed for convulsions (12). All of these patients had exhibited increased psychomotor activity due to various psychoses or to alcohol, barbiturate or opiate withdrawal. The drugs were given IV or IM in doses of 50 to 400 mgm. and at varying intervals for periods of one to seven days. In the alcohol withdrawal group, the incidence of grand mal seizures for the chlorpromazine treated patients was 9 per cent and for the promazine treated patients it was 7 per cent. This is less, though perhaps not reliably so, than the 12 per cent figure usually quoted for alcohol withdrawal states without tranquilizer treatment (47). However, neither of these figures takes into consideration previous epilepsy among the subjects and no electroencephalograms were taken after recovery to rule out persistent cerebral dysrhythmia. It is noteworthy that one of these promazine treated alcoholics, with severe delirium tremens, had never had a previous seizure and convulsed just five minutes after the last of a 700 mgm. IV dose of the drug was given.

In a series of 110 patients with full-blown delirium tremens given promazine, seizures occurred while on the drug in 10 per cent or 11 of the subjects. The dose employed was 200 mgm. IV initially followed by 100 to 150 mgm. orally every four to six hours (14). There are as yet no reported convulsive complications of reserpine in the treatment of the acute alcoholic states, though compared to the phenothiazines it has been relatively infrequently used to date.

*Summary:* Seizures occur in non-alcoholic non-epileptic patients while on tranquilizers. The effect of tranquilizers in epileptics, however, is controversial. Seizures occur in the acute alcoholic states treated with tranquilizers but it is unclear if this seizure incidence is significantly dif-

ferent from that in the untreated alcoholic states.

### CASE REPORT

The patient selected for this experiment was a 31 year old chronic alcoholic male who had been hospitalized some months earlier at University Hospitals for another research study in conjunction with the Cleveland Center on Alcoholism. He had experienced generalized seizures plus delirium tremens on two previous occasions, both occurring following alcohol withdrawal while in jail. The patient had been treated for these episodes at another local hospital, where the records verified the presence of auditory and visual hallucinations and disorientation at that time. He had never had a seizure prior to his alcoholism nor when not drinking and there was no history of epilepsy in the family.

Physical examination at the time of this patient's first admission revealed a thin, tremulous, minimally dehydrated white male with the odor of alcohol on his breath. Admission blood pressure was 210/88 and pulse was 170. At this time the patient was given 100 mgm. of chlorpromazine orally and three hours later was observed to have a grand mal convulsion. He then received dilantin and phenobarbital for four days and had no further seizures. The patient's blood pressure dropped to normal within several hours of admission and remained at normal levels throughout his hospital stay. Hemogram, urinalysis, liver profile, chest film, electrocardiogram, and electroencephalogram were without abnormalities. Hepatoscanning revealed multiple small defects suggesting a fibrotic component consistent with cirrhosis.

Following discharge from the hospital the patient promptly ran afoul of the law while intoxicated. After several months in the Work House, presumably with no alcohol ingestion, he was transferred back to University Hospitals to participate in the present experiment which lasted 37 days. Additional studies obtained at this time were BMR's of +12 and +10 and a repeat normal chest x-ray and electrocardiogram.

### METHODOLOGY

After base line electroencephalograms and routine laboratory work had been obtained, electroencephalographic tracings were taken following the ingestion of alcohol alone, alcohol plus one of three tranquilizers, and the drug alone. The patient's clinical status and blood pressure were recorded on experiment days and daily weights were obtained. Two fasting blood sugars were drawn prior to electroencephalographic recordings. Table 1 illustrates the procedure for the series of chlorprom-

TABLE 1

*Experimental Procedure for Chlorpromazine Investigation*

| Experiment | Hospital Day | Time of Administration | | EEG and Breath/Blood Alcohol | |
|---|---|---|---|---|---|
| | | Alcohol | Chlorpromazine | #1 | #2 |
| A1 | 5 | 12:40 P.M. | — | 2:00 P.M.* | 3:00 P.M. |
| | 6 | — | — | 9:00 A.M. | — |
| A2 | 9 | 12:40 P.M. | 1:30 P.M. | 2:00 P.M.* | 3:00 P.M. |
| | 10 | — | 8:00 A.M. | 9:00 A.M. | — |
| A3 | 13 | — | 1:30 P.M. | 2:00 P.M. | 3:00 P.M. |
| | 14 | — | 8:00 A.M. | 9:00 A.M. | — |

A1—Alcohol alone
A2—Alcohol plus chlorpromazine
A3—Chlorpromazine alone
* All blood levels were calculated from measurement of reducing substances in exhaled air. Asterisk denotes additional direct determination of alcohol in venous blood.

azine experiments. This protocol was repeated for the promazine and reserpine parts of the study. The rationale for the experimental design will be presented in the discussion section.

The alcohol was ingested as a single dose of 120 ccs. of 100 per cent (absolute) ethyl alcohol diluted half and half with fruit juice and consumed over a 20 minute period. Electroencephalograms were taken at one and two hours after the end of the alcohol ingestion, as well as the following day. The recording time for each tracing was about 20 minutes. Blood alcohol determinations were made either by analysis of venous blood or with the Breathalyzer Apparatus®[3], or both, just prior to each electroencephalogram for all experiments where alcohol was ingested.

When drugs were given it was both by parenteral route (on the first day, one-half hour prior to the first EEG) as well as orally (on the following day, one hour prior to the EEG; see Table 1). The dosage of chlorpromazine was 100 mgm. initially and this was raised to 200 mgm. in a subsequent experiment. The dosage of reserpine was 2.5 mgm. while promazine was given in 100 mgm. and later in 200 mgm. dosages.

The patient was kept in a fasting state except for the alcohol and/or drug on the morning of the experiments. One dosage of drug was tested each week, both with and without alcohol. The initial experiment following alcohol ingestion alone served as control for each drug experiment.

## RESULTS

A total of thirty electroencephalograms was obtained in the experiments with alcohol and the three tranquilizers. None of these were definitely abnormal. Some of the records showed mildly diffuse slowing characteristic of drowsiness. The patient showed no abnormalities of blood pressure as recorded throughout the experiment. Blood alcohol levels varied, on the day of alcohol ingestion, from 110 to 160 mgm. per 100 ml. one hour after ingestion, except for one Breathalyzer determination of 240 mgm. per 100 ml. (one hour after ingestion of alcohol without any drugs). A venous blood sample at this same time, however, was reported as 110 mgm. per 100 ml. Two hours after the ingestion of the alcohol, the blood level as determined by the Breathalyzer varied from 80 to 115 mgm. per 100 ml. The agreement between Breathalyzer and venous blood was always within 20 mgm. per 100 ml. except for the one time mentioned above. Two blood sugars, after alcohol-promazine and alcohol-chlorpromazine administration, were both 90 mgm. per 100 ml. Daily weights did not vary with any particular experiment.

As for the patient's clinical status; when he received the alcohol alone he became very hostile, but this was also the case when he received the alcohol plus tranquilizer. He became drowsy on alcohol plus promazine and chlorpromazine, but not on either drug alone. Several hours after the patient received alcohol plus reserpine, however, he became dyspneic, flushed, and experienced headache. This condition disappeared overnight. There were no evidences of slurred speech or abnormalities of gait following alcohol ingestion.

## DISCUSSION

It is known that alcohol withdrawal following chronic intoxication causes seizures, even in non-epileptics. Likewise seizures have been observed following the use of several tranquilizers. The combination of alcohol withdrawal *plus* tranquilizer administration is one that occurs often in the present day management of acute alcoholic crises. Experimentally, however, the chronic intoxication method is not practically applicable to concomitant testing of

[3] Stephenson Corporation; Red Bank, New Jersey. This apparatus estimates blood alcohol level by colorimetric measurement of reducing substances in exhaled air.

several tranquilizers because of the time required.

It was thus decided to use a single dose of alcohol for each part of the experiment. The amount selected for ingestion was 120 ccs. of 100 per cent (absolute) ethyl alcohol diluted with the same amount of fruit juice. This figure was based on intoxication experiments conducted at the Cleveland Center on Alcoholism (49). Their work with alcoholics revealed average blood alcohol levels of 190 and 165 mgm. per 100 ml. at one and two hours post-ingestion respectively. Over 50 per cent of alcoholics with these blood alcohol levels will show clinical evidences of intoxication (26). The percentage is higher when the moderate drinker or abstainer is involved (36). The blood alcohol levels obtained in our experiments were somewhat less than we might have expected from the data presented above, although a pilot study conducted before this experiment had resulted in blood alcohol levels of 105 and 115 mgm. per 100 ml. at one and two hours post-ingestion respectively (46). Our patient showed no evidences of clinical intoxication.

The three tranquilizers, chlorpromazine, promazine, and reserpine, were selected because they are the ones most commonly employed in the treatment of the acute alcoholic states and the literature is thus more complete in these areas. Doses were selected which are currently employed in the treatment of acute or "impending" delirium tremens (1, 12, 15, 16).

The timing of the initial day's electroencephalograms depended upon two facts. One observation is that the most pronounced electroencephalographic changes following alcohol administration usually occur at the time of maximum blood alcohol concentrations in alcoholic patients (24, p. 4). The other was that previous studies have shown that most of those patients who convulsed on chlorpromazine did so within two hours of an oral dose (44). Our patient, however, had convulsed three hours after an oral dose of chlorpromazine during his initial hospitalization.

SUMMARY

Clinical and electroencephalographic observations were made on a patient with "rum fits" who had also convulsed several hours after receiving an oral dose of chlorpromazine for "impending" delirium tremens. These observations were made after the experimental administration of alcohol and a tranquilizer (chlorpromazine, promazine, reserpine), alone and in combination.

No electroencephalographic abnormalities were recorded. The patient did become hostile when intoxicated and drowsy when receiving alcohol and a tranquilizer. No changes in clinical status were noted when the tranquilizer alone was given.

It would be most useful to find one particular tranquilizer effective for acute alcoholic crises and yet, in patients with low convulsive thresholds, which would not result in an increased seizure incidence. Further work is needed to elucidate the mechanism whereby the various tranquilizers acting alone, as well as in conjunction with alcohol, cause seizures in certain individuals.

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# PSYCHOTHERAPY WITH LYSERGIC ACID DIETHYLAMIDE

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If the question were asked, "What are the elements which might assist the psychotherapeutic process?", a number of desirable considerations would come to mind.

High on any list would be the wish to reduce the defensiveness of the patient and thereby resistance to the uncovering of repressed memories. An increased ability to accept conflictual material should also be associated with the reduction of defensiveness. This implies a lessening of guilt and self-depreciation, with an increase in the ability to view emerging problems with some detachment.

A further desire would be the achievement of an enhanced patient-therapist relationship. Other valuable characteristics would be that consciousness remain intact and that recall be amplified.

Recently in the psychopharmacological literature there has been considerable mention of an agent, lysergic acid diethylamide (LSD-25), which appears to achieve some of these goals.

Indications of the possible value of LSD-25 were personally noted in an earlier study (9) of the psychological test changes produced by the drug. Although reactions varied over a wide spectrum there appeared to be a general lowering of ego defenses and an intensification of interpersonal relationships with those individuals present. Some of the subjects described their experiences as psychotic, but others reported unusually pleasant and insightful sessions. A few believed that their experimental exposure to the drug had a sustained effect upon their subsequent behavior.

[1] The Neuropsychiatric Hospital, Veterans Administration Center, Los Angeles. The d-lysergic acid diethylamide and the 1-acetyl d-lysergic acid diethylamide used in this study were provided by Mr. Harry Althouse, Sandoz Pharmaceuticals. Supported by a grant from Mr. Ewing W. Reilley.

It was hypothesized that LSD-25 might be useful in a therapeutic setting as an aid in the uncovering and acceptance of unconscious material and might shorten total treatment time.

## REVIEW OF LITERATURE

The initial mention of LSD-25 as an aid to psychotherapy appears to be the paper by Busch and Johnson in 1950 (7). In their discussion of eight psychoneurotic cases they mention that the patients had experiences which "profoundly influenced the course of their progress." There was enhanced recall and a reliving of early traumatic episodes which permitted abreaction and increased insight into their conflicts.

Two years later Savage (24) reported on the treatment of 15 psychotically depressed patients as well as a control group. After treatments for a month with daily dosages of 20 gamma (20 micrograms) gradually increased to 100 gamma, the improvement rate was felt to be no better than for those on routine hospital activities alone. The author notes, however, that LSD-25 produced hallucinations which afforded valuable insights for the therapist into unconscious processes.

The next year Katzenelbogen and Fang (22) discussed the successful use of doses up to 50 gamma of lysergic acid diethylamide to facilitate interviews with 20 schizophrenic subjects. They reported that the "ventilation of emotion appears to be more marked with LSD-25 than with methedrine or sodium amytal."

Abramson has investigated LSD-25 from many aspects. Four articles (1, 2, 3, 5) deal with the facilitation of psychotherapy. He uses 20 to 40 gamma of the drug in patients who appear at a standstill in the course of treatment. Tape recordings of the

extended sessions demonstrate an interesting acceleration of the therapeutic progress. He notes that LSD-25 is characterized by pharmacologic safety, maintenance of the patient in a conscious and cooperative state, and by lack of evidence of addiction after repeated use (2).

Frederking (19, 20) reports on a series of 24 cases treated in his office with a dosage range of 40–60 gamma at intervals of several weeks with conventional therapeutic appointments in between. He notes that patients frequently re-experience scenes from their early life and feels this can have a lasting effect on certain psychosomatic illnesses such as constipation and dysmenorrhea. He speaks of the achievement of a dream-like state which can be advantageously analyzed. "Psychocatharsis" then follows. Frederking used both mescaline and LSD-25; he feels that the former produces a stronger emotional response but that LSD-25 has a broader spectrum of reaction.

Sandison, Spencer and Whitelaw (30, 31, 32, 33) have evolved a special technique and environment for LSD-25 treatments at Powick Hospital in England. A ward of the hospital is reserved for this project. Dosages begin at 25 gamma and increase weekly until 100–200 gamma are reached. On occasion as much as 400 gamma are given. The team consists of a psychiatrist in charge, nurses who are in attendance during drug sessions, and therapists who conduct group therapy apart from the drug experiences.

These investigators have recently reported on 94 patients with follow-up periods varying from six months to five years. Sixty-one of these recovered or improved, 32 failed to derive appreciable benefit, and one was lost to follow-up. Most of their patients were chronic neurotics resistant to prior therapeutic effort. Many were considered to be candidates for leukotomy. "We would stress that all our cases were in danger of becoming permanent mental invalids, lifelong neurotics or suicides." (32)

Further, they discuss a combined treatment with lysergic acid and chlorpromazine in 14 schizophrenics. In instances where the illness had existed for less than two years, encouraging results are described.

The authors conclude that LSD-25 appears to be of "utmost value in psychotherapy, both in cases otherwise resistant to treatment and as a method of avoiding the prolonged time necessary for a full psychological analysis." (33)

Denber and Merlis (13, 14) were the first to employ a combination of intravenous mescaline and chlorpromazine in a therapeutic setting. Twenty five of 40 acutely ill schizophrenic patients improved. Only seven of 17 chronic schizophrenics showed any benefit. It is their hypothesis that mescaline mobilizes anxiety which in turn drives the patient into symptom formation or symbolic productions which can then be interpreted. "Mescaline releases the repressing forces of the unconscious and permits a free flow of conflictual material hitherto kept out of awareness." (12)

There are additional studies of therapeutic experience with LSD-25. Anderson and Rawnsley (6), using the drug as a psychodiagnostic tool, mention that six of 19 psychiatric patients showed long-lasting favorable changes after very few treatments. Its use in cases of mental deficiency was explored by Davies and Davies (11). In doses of from 20 to 400 gamma memory was stimulated and the authors considered it to be an aid to treatment.

Langner and Kemp's brief report (23) mentions 500 LSD-25 sessions, but describes no specific technique. Encouraging results are claimed with neurotics, schizophrenics, manic depressives, and alcoholics. Feld, Goodman and Guido (18) have given 18 patients 52 treatments in 100–200 gamma amounts. They observe that "LSD-25 has the astonishing quality of bringing into focus the patient's repressed emotional attitudes, conflicts, etc., and permits their reactivation." All except those with chronic brain syndromes demonstrated some degree

of improvement in the sense that they were able to return to society and their families in a more productive capacity. Osmond (27), Ditman (16) and Hubbard (21) speak of the successful treatment of prognostically poor, chronic alcoholics with a brief series of LSD-25 sessions.

Martin (26), working with outpatients at a day hospital, describes the treatment of 50 chronic neurotic patients with gradually increasing doses of LSD-25 to optimal levels terminating the session with chlorpromazine. Special precautions were taken with respect to transporting and overnight care on treatment days. Forty-five patients showed immediate improvement; after two years nine had relapsed. Of these, the majority had chronic tension states. The author feels that "The therapeutic effect of LSD-25 would appear to be in the reliving of early experiences, particularly if accompanied by release of repressed feeling . . . the presence of the psychiatrist helps him to act out and work through the experience in an environment of security not present at the original experience."

In the most recent article to date, Lewis and Sloane (24) report on treatment of 23 psychiatric inpatients with results no better than obtained by other treatments. "Nevertheless, we concluded that the drug provided a useful aid to psychotherapeutic technique." They feel that the main value of LSD-25 lies in "the facilitation of transference phenomena and regression and increase of suggestibility."

The foregoing review of the literature suggests that: 1, LSD-25 lessens defensiveness; 2, there is a heightened capacity to relive early experiences with accompanying release of feelings; 3, therapist-patient relationships are enhanced; and 4, there is an increased appearance of unconscious material. Most investigators report that therapeutic benefit can occur through any one or more of these factors.

## METHOD

This exploratory study of the therapeutic possibilities of lysergic acid diethylamide concerns 22 patients who have been followed for a period of from six to 17 months. Of these, five were hospitalized patients and 17 were treated as outpatients. The diagnoses ranged through neurotic depressions, anxiety states, and character disorders to borderline schizophrenia. Weekly treatments were the rule, the initial dose being a 25 gamma tablet. This dosage was increased in 25 gamma increments until a level of 100 to 150 gamma was administered. With doses of 100 gamma or more, ampules of LSD-25 were added to distilled water and taken by mouth. Two patients who were resistant to the drug were given dosages in larger than 25 gamma increments, *i.e.*, 25, 75, 125 gamma.

On five occasions 500 gamma of ALD-52 (1-acetyl-d-lysergic acid diethylamide) was given, and once 500 gamma of MLD-41 (1-methyl-d-lysergic acid diethylamide). This amount appears to be equivalent to 200–250 gamma of LSD-25. Drugs were never administered more often than every third day because of the rapid onset of tolerance.

The gradual increase in dosage appeared to minimize unpleasant side effects. Anxiety was usually absent or minimal, and as the patient progressed to the higher dosage levels, deeper areas of the unconscious seemed to become accessible. With a few individuals, split dosages were given at the high levels when somatic disturbances or excessive anxiety had appeared at the previous session. All sessions were tape recorded.

The number of drug treatments ranged from one to 16, with a mean of 4.6. When the treatment series extended beyond four or five sessions, it was found efficacious to allow more than a week to elapse following treatments in which a good deal of significant material was uncovered. Non-drug in-

terviews with the therapist were found helpful, and therapeutic gains appeared to be integrated and consolidated when the patient listened to the tapes of crucial sessions.

Drug activity could be noted for four hours at the low dosages and for six to eight hours when 75 gamma or more had been administered. During most of this time the patient lay on a couch in a pleasant room with the therapist constantly in attendance. Lunch was available if the patient became hungry. Records were played initially to aid in relaxation. After repeated observations that music seemed to potentiate the drug action, it was used when there was no verbal exchange. Selections of the patient's choice or of a semi-classical nature were played during the early phase; certain piano concertos were used at the height of the experience.

In addition to music, other aids were found to assist in the therapeutic process. A mirror was helpful when difficult problems of self identification were being considered. Not infrequently the patient projected his unconscious concept of himself onto the reflection in the mirror. Family photographs, especially of spouse, parents and siblings, enabled the subject to externalize associated conflicts, and to re-experience repressed events with such vividness and force that they were repeatedly described as "relived." In this regard an interesting duality was noted. Although a childhood incident was being relived with appropriate emotional discharge, simultaneously it was also perceived by the patient from an adult perspective.

Toward the end of each session the patient was taken to the hospital art clinic to draw or paint whatever he desired. This was found to be helpful in continuing the therapeutic process and seemed to provide an opportunity to objectify subjective experiences.

The type of therapy performed in conjunction with LSD-25 varied according to the situation. Occasionally, the patient could clearly understand the problems and the defenses he had established even when these appeared in symbolic form. More frequently it was necessary to interpret the unconscious material deeply and directly as it arose. Such interpretations, which in conventional psychotherapy might have had devastating effects, seemed to be accepted without difficulty. One of the more important therapeutic actions was to direct the patient toward the frightening or painful symbolic material and to assist him in experiencing and understanding it.

Because of the unusual and extremely subjective nature of the experience, the therapist should have had personal experience with the effects of LSD-25. Ideally, he, too, will have undergone a series of increasing dosages. To a therapist who has not been through this process many elements of the patient's experiences will be unintelligible or misinterpreted.

## SELECTION OF PATIENTS

The most important factor in patient selection for LSD-25 psychotherapy is a genuine desire to get well. Our observation parallels that of Sandison (29) who considers motivation the single most important factor. Ego strength and intelligence are important, but motivating drive is primary and it must be more than looking for the magic of an easy way out. Not infrequently the more troubled the patient the better the prognosis since impetus to change may be greater. Often one or two drug sessions can be effective in enhancing motivation.

As can be seen from Table 1, improvement with LSD-25 therapy is not restricted to patients in any one diagnostic category. Individuals whose neuroticism is manifested by anxiety or compulsiveness did well. Those with depressive states appear to be very suitable, and those who have been unable to recover from a major situational

disaster are particularly amenable. As might be expected, the one patient with a predominantly traumatic neurosis showed dramatic improvement. Problem alcoholics selected for ego strength and motivation to change are excellent subjects.

The types not conducive to good results are the inadequate, schizoid personalities. Ineffectual, immature individuals who have never adjusted well cannot be expected to profit from short-term psychotherapy with LSD-25. Our experience with schizophrenics is too limited for inferences, and the literature is in disagreement on the subject. A further category of patients for whom the drug may be contraindicated has not yet been clearly delineated. This subgroup is described under the section on Potential Dangers.

Another group of people who benefited from the treatment cannot be said to be in emotional distress in the neurotic sense. These were unhappy and floundering individuals who had lost the ability to believe in anything or to identify with any concept larger than themselves. They seemed to benefit from the integrative aspect of a successful LSD-25 series. This integrative aspect, which is discussed under "Mode of Action" appears in one form or another to be an important contribution to the therapeutic end result of treatment.

### PATIENT-THERAPIST RELATIONSHIP

The relationship between therapist and patient is of crucial importance during therapy with LSD-25. Almost every investigator has emphasized the enhancement of transference which occurs. Generally, this was of a positive nature; however, it changed abruptly in two subjects to negative transference when especially disturbing material appeared. During the examination of these negative feelings the problems were resolved and abreacted. A straightforward discussion of both positive and negative transference situations is very helpful. This is not to be construed as an analysis of transference in the orthodox sense.

It is of greater importance that the approach of the therapist be flexible than that he be of a certain persuasion. He should be aware of the areas of unresolved conflict within himself so that these are not projected. Sensitivity, intuition, and the ability to make deep interpretations are important; the silent or reflective method does not take the patient as rapidly as possible to the core of his problems. A fear of premature or too penetrating interpretation is minimized by the patient's ability to view himself with detachment. Incorrect or unacceptable interpretations tend to be brushed aside

The therapy found to be most effective in this study has greatest similarity to the intuitive type used with schizophrenic patients (28). It is not surprising that a directive, personally-involved therapy which is applicable to psychotics, is effective here, too; LSD-25 states also involve dissolution of the ego, hallucinatory imagery, depersonalization, and other schizophreniform characteristics.

It was our impression that the therapeutic process was materially accelerated when both a male and female therapist was present. During periods of the intense experiences of previously-repressed affect or when ego disintegration was felt as a psychotic-like episode, the value of two therapists was especially apparent. They also served as stand-ins for inconsistent, manipulating, or rejecting parents and often became focal points of projected feelings.

### MODE OF ACTION

The manner by which LSD-25 produces its mental changes is obscure. It is known to be a strong serotonin antagonist, and serotonin is a synaptic transmitter in certain areas of the brain. However, other antagonists to serotonin, such as Brom-LSD (BOL), do not elicit the psychic phenomena characteristic of LSD-25.

Neurophysiological work by Marrazzi

and Hart (25), indicates that lysergic acid diethylamide inhibits the axodendritic synapse. If this is so, an hypothesis may be considered which could explain some of its cerebral activity. LSD-25 may inhibit the adaptive patterns of neuronal activity which are survival-oriented. It is postulated that many axodendritic circuits in the centricephalic system exist which sustain ego identity, reality orientation, and the mechanisms which defend us from psychic trauma. These circuits are presumably the ones which inhibit the primary psychic process. This primary state of psychic functioning is an undefended, undifferentiated, perceptually and cognitively unconditioned state. To protect against ego threatening situations and the impacts of psychic stress, much of the neuronal inflow is conditioned or blocked. Perception becomes modified toward a depreciation of the unimportant and a heightened awareness of the threatening. Fantasy gives way to practical and critical thinking. The ego boundaries become firmer; any threat to their integrity is met with a variety of defensive maneuvers. The inhibition and conversion of anxiety fosters psychic survival despite the fact that these processes may eventually become diseases of adaptation in their own right.

Drugs like lysergic acid diethylamide may temporarily check the manifold restraints which must occupy much of the work of the mind. The physiologic device of using inhibitors upon inhibiting systems is not uncommon in maintaining homeostasis. Insulin, for example, does not work upon any substrate directly, but inhibits the inhibitory effect of the anterior pituitary hormone.

This hypothesis is comprehensive enough to explain the purity of perception, depersonalization, autistic thinking, dissolution of the defensive structure and other phenomena noted in LSD-25 subjects.

With small doses (25–50 gamma) ego defensiveness and anxiety are lowered. The recall and "reliving" of past events is enhanced; frequently whole sequences unroll before the patient's eyes as though they had been stored on microfilm. Although he feels part of the scene, there is, in addition, a certain detachment as noted also by Sandison and Frederking (20, 32). When larger amounts are taken, symbolic, primal, and archetypal material often emerge.

With the uncovering of critical problems varying degrees of somatic discomfort and anxiety are felt. These may culminate in psychotic-like episodes, experienced symbolically as terrifying, overwhelming, or excruciatingly painful. The word most commonly used by the patient after an experience of this sort is that he feels "purged."

As the problems are worked through, the patient may undergo an integrative experience. In this context an "integrative experience" is used to describe a state wherein the patient accepts himself as he is, and a massive reduction in self-conflict occurs. There is a feeling of harmony with his environment and an upsurge of creativeness. At times this is perceived as a fusion of subject and object.

The integrative experience should be described further because it has not been a matter for scientific scrutiny and the semantic difficulties are considerable. There is usually a perceptual component which consists of looking upon beauty and light. Affectually, there is a feeling of great relaxation and hyperphoria. The patients describe an insightfulness into themselves, an awareness of their place in the environment, and a sense of order in life. These are all fused into a very meaningful episode, and it is believed that this can be significantly therapeutic.

For therapeutic gains to continue, the advances made during therapy must be acted upon. A person may achieve excellent insight only to slip back because his lifelong patterns of rejection and denial are used to avoid the acceptance of mature

responsibilities. Continuing psychotherapy is valuable here in the restructuring of habit patterns.

On the other hand, individuals who are highly motivated to change make rapid strides. One such patient, considered to have a serious personality disorder, was interviewed nine months after treatment. He had continued to improve in the interval although no therapeutic contact had occurred.

At some time following completion of the LSD-25 series, additional drug sessions may prove advisable. The detection of still unresolved conflicts or an encounter with some extraordinary life stress may be an indication for another session or two. In dependent individuals and some alcoholics, periodic but more-widely-spaced treatments may seem advisable. According to our observations optimal use of LSD-25 appears to consist of drug treatments spaced within the framework of ongoing psychotherapy.

### POTENTIAL DANGERS

Lysergic acid diethylamide is a potent psychoactive agent. The dangers involved with its use are not related to pharmacological toxicity. We are inclined to believe, along with Sandison (33), that the possibility of suicide may be a real hazard, as it is in the treatment of any serious mental illness. From our experience and that of other workers, this danger appears to be restricted to the higher dosage levels—those above 75 gamma—and an unfamiliarity with the drug.

Stoll (38) has mentioned two suicides which occurred in Europe following the experimental administration of LSD-25. In one case the subject was given the drug without her knowledge. One of Savage's (36) schizophrenic patients committed suicide shortly after LSD-25 "shattered her defenses" and "mobilized the supreme resistance."

Personal contacts with therapists using LSD-25 have turned up other cases of suicidal preoccupation and of actual suicide.

We have observed that a transient depression sometimes follows an LSD-25 session. This may be due to several factors: (1) the inability to integrate all of the unacceptable traumatic material uncovered during the session; (2) the feeling that the necessary effort is too great to be undertaken; (3) "coming back to earth" after a transcendental experience. It is therefore important that some sympathetic person be with the patient during the evening following treatment.

A more serious type of depression has been observed to occur when insights acquired under the drug are not translated into the life situation. It almost appears that if the clearly-indicated step forward is not taken, ground may be lost, followed by depression. In such cases additional therapy seems almost mandatory.

To give a patient who is incapable of handling his present load a defense-shattering drug like lysergic acid diethylamide raises the question as to whether a psychotic breakdown might not be precipitated. The fact that this has not yet been recorded is probably a reflection upon some of our theories of mental illness. On the other hand there is the real but remote possibility that a non-psychotic patient whose major defense is paranoid thinking may be moved by LSD-25 into the direction of further grandiosity. We have reports from other therapists of psychotic episodes which were controlled with chlorpromazine.

While none of our patients approached a treatment-precipitated psychosis, one case was indirectly observed. A patient with a compulsive personality, after five years of analytically-oriented therapy, had two LSD-25 sessions of 50 and 100 gamma with his own therapist. A reaction resembling paranoid schizophrenia ensued, although the patient's level of functioning was not impaired. On the contrary, previously unsuspected artistic creativity broke through in the form of song writing and a novel of some merit. However, systematized de-

lusions in the religious area and surrounding the drug itself persisted.

One of our hospital patients ignored conflictual problem areas under the drug and experienced only the feeling of oneness with his environment. He began to act superior in a grandiose way and was then deliberately directed toward the painful resolution of his walled-off conflicts. He undertook this very reluctantly, but with subsequent substantial therapeutic results.

A further instance, not included in the series, was observed much like the above-described hospital patient. The therapist had to force the patient to face conflictual material. The three individuals mentioned above appear to have a common ability to encapsulate unpleasant material along with an ease of access to what they interpret as cosmic levels. This type seems to be an exception to our impression that the integrative experience occurs therapeutically toward the end of a series. Since it is difficult to identify such people, caution in the selection of patients for LSD-25 is indicated. Furthermore, until these aberrant reactors to LSD-25 are more readily identifiable, high dose sessions should be performed on an inpatient basis.

None of our patients required termination of their LSD-25 reactions with a phenothiazine because of intolerable affectual discharge. When heightened anxiety or depression occurred in the post-drug period, it was handled by phone or additional interviews. There is no objection to the use of ataractics for palliation of excessive tension and anxiety between sessions.

As to LSD-25 addiction, the literature makes no mention of psychological habituation, nor can any be reported from our experience. The very rapid onset of a complete tolerance makes addiction in the ordinary sense of the word an unlikely development.

Elkes (17) mentions the possibility of delayed and serious after-effects following LSD-25 treatment, likewise Sandison (33) and Martin (26) speak of a brief return of the LSD-25 state spontaneously up to a year later. We have also observed the appearance of LSD-like phenomena spontaneously in patients at varying intervals following treatment. These spontaneous occurrences were welcomed by our patients as relaxing and beneficial. In other cultures experiences such as minor depersonalizations are not regarded as fearful or abnormal, but are highly valued.

It is hypothesized that the process initiated by LSD-25 in which unconscious material becomes more available, also lowers the threshold for the subsequent emergence of such material. Favorable conditions seem to be: moments of extreme relaxation, unusual stress, the limited environment or solitude, and also meditation-like, hypnagogic, and allied states. It is our impression that when a patient has developed a new frame of reference the spontaneous appearance of unconscious material becomes quite acceptable and is not to be considered hazardous.

A last potential danger arises from the impairment of motor coordination. Patients should not attempt to drive a car until the drug effects have worn off. It is self-evident that the drug should be administered only under medical supervision.

## RESULTS

Table 1 presents data concerning the patients by sex, age, number of sessions, dosage, diagnosis, and results. The difficulties inherent in assessing psychotherapeutic improvement are not restricted to this study. We tended to discount the subjective report of the patient, and only when objective evidence of a better situational adjustment was obvious was the term "improved" used. The development of more mature behavioral patterns and increased ability to cope with stress were evaluated during a follow-up period of six to 17 months.

Our own evaluation, plus that of the patient, was supplemented by the report of

TABLE 1
*Data on LSD-25 Treated Patients*

| | Sex | Age | LSD-25 Sessions | Dosage (Gamma) | Diagnosis | Results |
|---|---|---|---|---|---|---|
| 1. | F | 47 | 5 | 25, 50, 75, 100, 100 | Depressive reaction; in narcissistic personality | Improved |
| 2.* | M | 35 | 4 | 25, 50, 100, 125 | Passive-aggressive personality, passive; Hospital Diagnosis: Schizophrenia | Unimproved |
| 3. | M | 42 | 3 | 25, 75, 100 | Borderline schizophrenia | Improved |
| 4.* | M | 31 | 6 | 25, 50, 75, 100, 150, 500 ALD | Conversion reaction in a passive-aggressive personality | Improved |
| 5. | F | 59 | 3 | 25, 75, 100 | Depressive reaction in narcissistic personality | Improved |
| 6.* | M | 34 | 6 | 25, 75, 125, 150, 150, 500; ALD | Chronic anxiety reaction with alcoholism. Passive-aggressive personality | Improved |
| 7. | F | 60 | 3 | 100, 75, 100 | Emotionally unstable personality | Improved |
| 8. | M | 31 | 1 | 25 | Hysterical personality | Improved |
| 9. | M | 33 | 4 | 25, 50, 75, 100 | Passive-aggressive personality | Improved |
| 10. | F | 39 | 2 | M/A†, 25 | Depressive reaction in an emotionally unstable person | Unimproved |
| 11. | M | 57 | 5 | 25, 100, 25, 25, 25 | Inadequate & schizoid personality | Unimproved |
| 12. | F | 45 | 3 | 50, 25, 50 | Passive-aggressive personality | Improved |
| 13. | F | 21 | 6 | 25, 75, 125, 100, 250, 100 | Depressive reaction in a passive-aggressive personality | Improved |
| 14. | M | 47 | 2 | 100, 25 | Compulsive personality | Improved |
| 15. | M | 36 | 3 | 100, 25, 75 | Compulsive personality | Improved |
| 16. | M | 44 | 2 | M/A†, 25 | Emotionally unstable personality | Improved |
| 17. | M | 47 | 16 | 25, 50, 75, 50, 75, 75, 100, 100, 100, 125, 125, 100, 500 ALD, 500 ALD, 500 MLD, 200 | Inadequate & schizoid personality | Unimproved |
| 18.* | M | 51 | 4 | 25, 50, 75, 100 | Chronic anxiety reaction with alcoholism in a paranoid personality | Unimproved |
| 19. | F | 22 | 3 | 25, 50, 100 | Hysterical personality | Unimproved |
| 20.* | M | 33 | 4 | 25, 50, 75, 100 | Chronic anxiety reaction with alcoholism precipitated by gross stress | Improved |
| 21. | M | 40 | 6 | 50, 100, 100, 150, 500 ALD, 200 | Compulsive personality | Improved |
| 22. | F | 42 | 4 | 25, 50, 100, 100 | Depressive reaction | Improved |

* Hospital patient
† M/A—Mescaline 20 mg plus amphetamine 10 mg.

someone in close contact with him. To be considered "improved", all three judgments had to agree.

It will be noted that of the 22 patients 16 are considered to have improved. Of the failures, two were inadequate, immature personalities. One did not complete treatment. The second, despite the acquisition of important emotional insights, was unable to restructure his lifelong, ineffective reactions to people and situations. A third unimproved subject was a hospital patient with a diagnosis of schizophrenia. Three of the unimproved patients showed substantial

initial improvement. This was not sustained or consolidated by changes in habit patterns. One, an emotionally unstable person who had suffered from severe depressions, would not finish the treatment series; another, an hysterical personality, also had an incomplete series because of unrelated circumstances. The last, a hospital patient with a diagnosis of chronic alcoholism in a passive-aggressive personality, after a seemingly good adjustment following discharge, began drinking again and revealed paranoid attitudes.

It is possible that more extended therapy with LSD-25 would salvage an occasional failure. We agree with Sandison's (33) and Lewis and Sloane's reports (24) that if improvement is not achieved within four months long term treatment with or without the drug is indicated.

## DISCUSSION

In this exploratory study an attempt was made to determine whether a short series of LSD-25 treatments combined with psychotherapy could produce favorable changes in individuals with a variety of neurotic and/or character disorders.

While the difficulties of assessing change are self-evident, and the follow-up period is insufficient to establish long-term effects, the initial results of this therapy are encouraging. Two sub-groups appear to be emerging from the "improved" sample as the period of observation lengthens.

The first group consists of patients, who, on the whole, are maintaining their therapeutic gains and who tend to use former ineffectual methods of solving problems less frequently. These individuals have contacted us from time to time for help with a current problem. For them, perhaps, greater benefit would have occurred from more widely-spaced LSD-25 treatments within a therapeutic matrix.

The second group is smaller but more impressive. These patients have continued to move toward emotional maturity and have consistently attempted to restructure their patterns of behavior by themselves. They have shown no evidence that additional therapy is necessary.

While certain techniques have been described in this article, and certain aids have been discussed, it is possible that these methods are a reflection of the personality of the therapist. Additional techniques should be considered and explored; there are a number of possible approaches and the parameters of the action of LSD-25 are by no means clearly defined. As mentioned earlier, it appears a particularly suitable agent for insertion at strategic points in the course of individual psychotherapy.

From this study, as from the body of literature, the importance of lysergic acid diethylamide emerges as a facilitator of recall and as an aid in the abreaction of traumatic events, whether suppressed or repressed. It also serves to enhance patient-therapist relationships. It, along with certain other hallucinogenic drugs, is unique in that the patient remains lucid throughout the period of activity.

Another possibly important facet of LSD-25 treatments, as yet not clearly defined, is what we have described as the integrative effect. Stevenson (37) describes several types of experiences bearing on this. In our sample this integrative aspect appeared to occur in conjunction with resolution of conflicts. Perhaps when the synthesis of successful psychotherapy is understood as well as the analysis, therapeutic benefit may become more consistent.

For the therapist, the researcher, and the individual interested in human dynamics, lysergic acid diethylamide is extraordinary if only because of the rich view of the unconscious which it permits. Not only are varying depths possible with increasing dosages and number of sessions, but the ability of the patient to follow his own associations along with the interpretations of the therapist permits a dramatic opportunity to trace a problem to its origin.

Further, the outpouring of symbolic material, the lightning-fast chain of associations, the recovering of repressed elements, and the appearance of unusual phenomena present an unrivalled opportunity to confirm certain psychodynamic theories and to obtain data contrary to others. Further studies of a controlled nature should go far toward validating present tentative hypotheses and offering additional ones of human motivation and unconscious processes.


## SUMMARY

A series of 22 individuals, five of whom were neuropsychiatric hospital patients and 17 outpatients, with problems ranging from depressive states to borderline schizophrenia, were treated with an average of four or five weekly LSD-25 sessions. Dosages started at 25 gamma and built up to 125 gamma in 25 gamma increments. In a few cases the equivalent of 250 gamma was used. Sessions lasted from four to eight hours, music was played to facilitate the drug action, and aids such as photographs and a mirror were employed. One therapist was in constant attendance but during stressful periods the presence of both a man and a woman therapist appeared to speed the process. Improvement was judged by agreement among the two doctors, the patient, and the person closest to him. Follow-up interviews were held over periods ranging from six to 17 months. The important criteria of benefit was continuing success in behavioral adaptation. Improvement was noted in 16 out of the 22 cases.

A review of the literature was given, selection of patients was described, and the enhancement of patient-therapist relationship was discussed. Heightened rapport makes possible more penetrating interpretations and a more rapid approach to basic problems. The obscure mode of action of LSD-25 was speculated on as possibly being the inhibition of inhibiting neurophysiological systems which in turn facilitates the reappearance of forgotten memories, the recovery of repressed events, and the access to deeper, more symbolic material in the unconscious. An additional, apparently therapeutic, aspect of the drug action was noted which seemed to make possible an experience of integration for the patient wherein he was able to see himself in proper perspective and in relation to his environment.


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# THE APPLICATION OF TRIIODOTHYRONINE IN THE TREATMENT OF MENTAL DISORDERS

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The effect of the thyroid on emotional and mental states has long been noted. In 1949 Asher (1) reported that patients with myxoedema may have emotional and mental disturbances which could be mistaken for psychoses and he suggested that there may be many such patients in mental hospitals. In 1953 M. Reiss and his associates described the effect of the thyroid gland on psychiatric illness (16). Using the $I^{131}$ uptake test in 100 psychiatric patients, these investigators found that about 20 per cent had abnormal responses. They also found that in a significant number of patients, improvement in thyroid function was accompanied by mental improvement. In 1954 Watson (17) described the hypometabolic state as a clinical entity and noted its presence in 1.3 per cent of all patients admitted to a general medical service. He drew attention to the fact that the physiological cause of hyopmetabolism is often overlooked by physicians, but that its signs and symptoms are sometimes ascribed to psychoneurotic, anxiety-neurotic or hypochondriac states. In 1955 Kurland *et al.* (10) described the syndrome of non-myxoedematous hypometabolism as having the signs and symptoms of fatigue, headache, irritability, diminished sexual potency in men and menstrual irregularity in women, ill-defined skeletal pain, lethargy and emotional instability. The terms "metabolic insufficiency" (14) and "hypometabolic syndrome" (9) have also been applied to this clinical picture. Considered by an endocrinologist this group of signs and symptoms might lead to a diagnosis of hypothyroidism; considered by a psychiatrist they might lead to a diagnosis of a depressive state or even Melancholia.

Liothyronine (3,5,3′ L-triiodothyronine) was identified by Gross and Pitt-Rivers in 1952 as the natural direct and rapid acting thyroid hormone. These investigators concluded that L-thyroxine has to be converted to Liothyronine before it can exert its physiological effect at the cellular level (11). Liothyronine is between three and seven times as potent as L-thyroxine and is more quickly absorbed and utilized than L-thyroxine. It has also been reported to be effective in patients who fail to respond to therapy with desiccated thyroid or L-thyroxine (2, 4, 5). The good responses reported with Liothyronine for patients suffering from emotional and mental disorders associated with hypometabolism, led the writer to try Lio-thyronine (in the form of Cynomel; called Cytomel in the United States) with 24 patients, the majority of whom had been diagnosed as having depression or melancholia, but whose condition suggested hypometabolism.

The following case histories are representative of the responses observed.

## CASE HISTORIES

*Patient No. 1*, a 68 year old man, was hospitalized for observation and treatment after an attempted suicide in September, 1956. He had jumped into the sea with stones tied to his feet. On admission to the hospital he was self-absorbed, retarded, depressed and thought life was not worth

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living. A diagnosis was made of Recent Melancholia of the senile type. Electroplexy was tried but the patient proved highly sensitive to relaxant drugs, his breathing stopped and he required artificial respiration for three hours. A trial with Lio-thyronine was begun.

The patient was given 15 mcg of Liothyronine daily in 5 mcg doses after each meal. He showed an improvement, was less depressed and more active and alert. After two weeks the dose was increased to 30 mcg daily and his improvement became more marked. After four weeks it was possible to reduce the medication to 15 mcg daily.

The patient's first signs of improvement were physical. His complexion improved, he became more agile and his movements were quicker. While these physical signs were taking place, his mental state also improved. His depression subsided, he became alert, more interested in his surroundings, more cheerful and confident. Two and a half months after admission he was discharged on a maintenance dose of 15 mcg daily. A report received two months later stated that his improvement was maintained.

In May, 1957 he lost his abode which he had occupied for 30 years. A few days later he was admitted to the hospital for the second time. Although he was depressed and retarded, on the whole his condition was better than on his first admission. He stated that for some weeks he had not been taking tablets.

The patient was given 15 mcg of Cytomel from the first day of readmission and 10 days later it was possible to transfer him to the Convalescent Unit, where he remained cheerful and felt quite well.

*Patient No. 2*, a 74 year old asthenic man, resided at a nearby hotel to be near his wife, a patient at this hospital. In October, 1956, in a bout of depression, he attempted suicide by cutting his wrist. He was hospitalized with the diagnosis of Recent Melancholia. Tranquilizers produced a slight improvement during the first week, but this was slow. In the second week Liothyronine, 15 mcg daily, was given instead. After three weeks on Cytomel the patient showed so much improvement that he no longer required special observation. He was up and about, showed insight and regretted his deed. He became cheerful and his depression subsided. He was transferred to the Convalescent Unit where he reached a satisfactory level. He was discharged in April, 1957 and now resides in a local boarding house. He is as well now as on discharge; has a small daily dose of 5 mcg Cytomel and has been heard to say "I feel better now than for the past 20 years."

*Patient No. 3*, a 64 year old man, has a medical history dating back seven years. He was admitted to St. Lawrence's in July, 1950 suffering from Confusional Psychosis. At that time he was treated with male hormones and responded well. He was discharged in November, 1950 on a maintenance dose of Testosterone.

In July, 1955 he was readmitted with a diagnosis of Melancholia. After a course of Modified Electroplexy he was able to take his voluntary discharge in October, 1955.

In January, 1957 he was admitted for the third time. The diagnosis was Recurrent Melancholia and he was given a course of Electroplexy. He improved once more but this time not to such a degree as to permit his transfer to the Convalescent Unit. In February, 1957 he was given 15 mcg Liothyronine daily and promptly showed a marked improvement. This was held at a satisfactory level upon his transfer to the Convalescent Unit in March, 1957. The following month he was discharged from the hospital on a maintenance dose of 10 mcg Cytomel daily.

*Patient No. 4* was a man of 49 who, on admission, looked older than his age. He was obese, hard of hearing, and with a dry skin. Being dull, disinterested and retarded

he made the general impression of a mental defective. He was solitary, lacked initiative and energy and displayed vague persecutory ideas. Diagnosis was Melancholia and he was regarded as intellectually subnormal. Since his symptoms were suggestive of hypometabolism, he seemed a likely candidate for Lio-thyronine therapy and treatment was commenced soon after admission. For the first two weeks he received 10 mcg daily, after that 15 mcg. He became more interested in his surroundings, more alert and quicker in response; his depression gradually subsided. The dosage was increased to 30 mcg daily after four weeks' medication and to 40 mcg two weeks later. At the end of two and one-half months he was behaving sensibly: he conversed willingly and rationally and said he "felt better than for a long time." After a few months in the Convalescent Unit he was discharged on a maintenance dose of 30 mcg Cytomel daily and now works in his father's shop as an outfitter.

*Patient No. 5*, a 29 year old man, was admitted to the hospital in February, 1957 for observation with a diagnosis of depression. He was dull, retarded and lacked initiative and energy though he was fairly cooperative and psychotherapeutically approachable. During the first four weeks of hospitalization he made a steady but slow improvement and at the end of this period he was transferred to the semi-convalescent ward. There he was employed on light ward duties, but remained a dull and evasive worker. After four weeks of observation on the ward Lio-thyronine therapy was commenced. For two weeks he was on 10 mcg Cytomel daily; then the dose was doubled. He became more cheerful and contented and improved sufficiently to be transferred to the Convalescent Unit. He felt quite well, became quicker in conversation and even witty. At the beginning of May 1957 he thought himself capable of returning to his previous occupation and was discharged. The report from the Mental Health Worker who visited him after discharge stated, "Has made good progress and is very much better since becoming a patient at the hospital. His mother is very pleased with his improvement. The patient will attend an outpatient clinic, though feels no need for it if his progress continues." His maintenance dose was 10 mcg Cytomel daily; he did not attend the outpatient clinic.

*Patient No. 6* was a manual worker, 54 years old. In his youth he had been an athlete, but now suffered from a bilateral inguinal hernia which prevented him from being active and handicapped him in his heavy manual work. This disability worried him considerably. On his admission in January, 1956 he looked older than his age, was preoccupied with his bodily condition and subsequently depressed. The diagnosis was Melancholia, moderate, partly involutional. Therapy with male hormones improved his condition. A combination of Electroplexy and tranquilizers helped still further and he was transferred to the Convalescent Unit. After four sessions of Electroplexy he was discharged, to continue the treatment as an outpatient.

One year after the first admission, in January, 1957 he was admitted in almost the same state as a year previously. Two sessions of Electroplexy improved his condition and he was transferred to the Convalescent Unit for a trial. A herniotomy has not been performed and the patient remained preoccupied with his physical state and mildly depressed. Cytomel was begun at 5 mcg daily, increased after a short time to 10 mcg. After two weeks on 10 mcg daily he became cheerful, quite contented and went home for a weekend. On his return he volunteered for gardening work saying he "could do it wearing a truss". He was gardening then, feeling fairly happy and remained cheerful and contented waiting for his operation. This was performed in August, 1957 and the patient made an uneventful recovery. Six weeks

after the operation he went home on a maintenance dose of 5 mcg Cytomel daily.

*Patient No. 7* a 54 year old man, has been an inpatient at the hospital on three occasions. First admission was in February 1953 with a history of depression. He stayed two months, underwent a Prolonged Narcosis and left the hospital improved. His second admission was in November, 1955. The diagnosis was Recurrent Depression. This time Prolonged Narcosis failed to improve him markedly and it was followed by Electroplexy. He responded to this treatment not badly, but became apprehensive towards it and took his voluntary discharge prematurely in February, 1956. The patient was admitted for a third time in March, 1957. He was given a short course of Electroplexy followed by tranquilizers. The improvement remained only moderate. The change to antidepressants did not make a marked difference in his condition. In May, 1957 a trial was made with Cytomel: 10 mcg daily. The response was prompt. He became more lively, more interested and more contented. The dose was increased to 15 mcg daily and in June, 1957 he was discharged on a maintenance dose of 10 mcg daily.

*Patient No. 8*, a man of 65, has been treated here on two occasions. The first time was in 1956, for moderate depression. He improved under tranquilizers during a stay of six weeks. He was readmitted in February, 1957. After a short course of Electroplexy the patient improved and the improvement was maintained with tranquilizers. In April, 1957 Lio-thyronine was substituted for the tranquilizers. He was given 10 mcg Cytomel daily. There was a definite increase in the rate of his improvement. He felt and was cheerful, alert and witty. A maintenance dose of 5 mcg daily was found sufficient. Two months after the commencement of Cytomel-therapy he was discharged from hospital.

*Patient No. 9*, a young athletic man, 30 years of age, suffers from Schizophrenia. His first admission was in 1954. At that time he was treated with Electroplexy and was discharged on trial after he gained a fair remission and after a stay of five months.

In April, 1957 he was readmitted. He appeared somewhat better than on his first admission. However, he was introverted, solitary, disinterested and had vague and bizarre ideas. Psychotherapy with aid of tranquilizers improved his behavior, but he remained dull and retarded. A trial was made to add Lio-thyronine to his tranquilizers. He was put on 5 mcg Cytomel twice daily (mornings and afternoons) with Chlorpromazine 100 mgm at noon. This regime produced an improvement in his condition and the dose was increased to 10 mcg. Cytomel twice daily without increase of the tranquilizer. His dullness gave way to a fair degree of alertness, he showed more insight and less introversion and his interest in happenings and surroundings increased. Chlorpromazine was omitted from his medication for two days, but he complained that he felt "hot, lightheaded and inclined to agitate." At present he is on a maintenance dose of 5 mcg Cytomel mornings and 25 mgm of Promazine Hydrochloride at noon and at teatime. The patient feels quite well, is in the Convalescent Unit, works well with other patients with whom he mingles freely, has resumed his weekend paroles at home and would like to get a job in his own trade as a carpenter.

*Patient No. 10* is a man of 49, a clerk of the pyknic type who has been suffering from moderate depression for a considerable time and who has attended the writer's outpatient clinic for over two years. Throughout the treatment he has been able to continue his job. Professionally he had some disappointments; with his domestic life he is quite contented. He had many types of ambulant treatment for he usually got used to medication and responded favorably to a change if it were accompanied by psychological reassurance. The latest change has

been to Cytomel and for the first time he seems genuinely improved. "This time", he said, "you hit the jackpot. I feel better than for years." He was discharged from regular attendance at the clinic.

## DISCUSSION

From numerous reports on the influence of the endocrine glands on brain function it appears that the main glands involved are the thyroid, the gonads and the adrenal. Thus it is hardly a coincidence that the main groups of mental disorders are connected with those periods in life at which the endocrine system undergoes changes: puberty, Schizophrenias; middle and old age, depressions, Melancholias, involutions and dementias; during pregnancy, childbirth and lactation, brief manic and confusional psychoses.

When the change in the endocrine system affects the thyroid and the utilization of its hormones, so as to produce the state of hypometabolism, the mental symptoms connected with it may well be due to inadequate oxygenation in the brain. That a deficiency in oxygen will cause a deviation from normal brain function is shown by the well known behavior of pilots at high altitudes and with inadequate oxygen supply. The pilot will feel confident that his mind is clear and his judgment sound; he is entirely unaware of the alteration in his behavior. Thus he shows a definite loss of insight—the most characteristic feature in mental disorders (13, 15). Similarly people living in high altitudes are reported to show disorders of memory, concentration and emotional stability (8), equally characteristic signs in mental disorders. The special interest of Lio-thyronine in psychiatry is, first, that by increasing metabolism it can increase the consumption and utilization of oxygen at the cellular level (12). Second, it appears to have a special affinity to and a positive effect on the gonads (7, 9, 11). Finally, in contrast to Thyroxin Liothyronine prevents adrenal atrophy in thiouracil-treated rats: thus it apparently acts as a synergist of the adrenal gland. Liothyronine seems to act in three directions each of which may have a beneficial effect on the brain metabolism and subsequently on the brain function. It increases the consumption and utilization of oxygen; it stimulates the function of the gonads and of the adrenal gland. It should be stated that a patient's response to Lio-thyronine does not of itself prove the presence of hypermetabolism, since it is probable that the hormone exerts its beneficial effect in the presence of normal thyroid function. Flach *et al.* (3) for example, has observed that Lio-thyronine produces beneficial effects in schizophrenic patients with depression who had no evidence by laboratory tests of hypothyroidism.

## SUMMARY AND CONCLUSION

It sometimes happens in a psychiatric service that patients with hypometabolism are treated symptomatically for depression, while their thyroidal metabolic state is overlooked. It is understandable that this should occur since the general lassitude, irritability, somnolence and decreased mental alertness which often accompany hypometabolism may be the major complaints of the patient and the reason he is brought to the attention of the psychiatrist. In the ten patients here described, for example, these psychic symptoms predominated. An empirical trial with Lio-thyronine quickly brought about an improvement in their condition. The good responses may have resulted from a correction of a hypometabolic state showing symptoms common to both the depressive and the hypometabolic condition. Of the ten patients, only two remained in the hospital. Of the 24 patients treated with Cytomel during the period from September, 1956 to September, 1957, 17 were discharged and the majority of the remainder are improved. Of the 17 discharged patients, 15 remained out of the hospital one year or more after discharge. Since Lio-thyronine

acts more quickly than Thyroxine, is absorbed and eliminated more quickly and its activity is much more potent than Thyroxine's (6), it is superior to desiccated thyroid or L-thyroxine for empirical trial in psychiatry. In the doses used no untoward effects were encountered during and after the trial.

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# SOME EFFECTS OF A NEW PSYCHOTOGEN IN DEPRESSIVE STATES[1]

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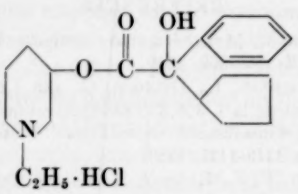
A group of 3-N-substituted piperidyl benzilates have been recently demonstrated to possess psychotomimetic properties (1, 6). The N-methyl-3-piperidyl benzilate, in dosages of 5–10 mg orally, produced distinct auditory and visual hallucinations in every normal individual tested. The hallucinations lasted for many hours, and were accompanied by gross distortion of visual perception and by a confusional state corresponding to delirium. A number of subjects exhibited paranoid ideation and ideas of grandeur, while others suffered a complete loss of contact with the environment and frequently reacted to their hallucinations. When the toxic symptoms disappeared, the subjects experienced a marked physical weakness for 10–24 hours, after which period they regained their pre-experimental status.

*It was noticed, however, that some of the normal volunteer subjects developed a change in their basic mood and drive. This change usually appeared 24 to 48 hours after the physical weakness disappeared. The newly emerging modulation of mood can be characterized as slightly hypomanic and of increased drive. This last observation indicated that the drug might be useful in the treatment of psychiatric states in which the outstanding symptom is a depressed mood.*

In the course of examining the structure-activity relationships of various congeners of the piperidyl benzilates (2), it was found that substitution of a cyclopentyl for one of the phenyl groups in benzilic acid considerably enhanced psychotogenic potency and greatly prolonged the duration of action. The compound, designated JB–329, has the following structure:




N-ethyl-3-piperidyl cyclopentylphenyl glycolate hydrochloride.

This derivative also seemed to produce considerably more hyperactivity and central stimulation than did its benzilate congener. The present communication concerns the use of JB–329 on psychiatric patients.

*Case No. 1.* The first patient was a 60 year old man, a former bricklayer, who had been hospitalized for the last ten years. Examination revealed his case to be one of severe depression with suicidal tendencies, caused apparently by the neurotic reaction of his burned-out body to the insoluble problem of his wife's psychotic illness. The patient was given 12 mg of JB–329, and within an hour showed signs of confusion, drowsiness, ataxia, and hypereflexia. A few hours later he began having hallucinations, was disoriented, extremely restless, and beginning to lose contact with the environment. Autonomic symptoms were present throughout, such as mydriasis, tachycardia, dryness of the mouth, and muscular weakness. At the end of 24 hours, he seemed considerably less depressed, smiled, laughed, and was much more talkative, although he professed to be just as depressed as he was before the treatment. Psychological reexamination with the Edwards and Rorschach

[1] Aided by grants from the Mental Health Fund, State of Illinois, and the Teagle Foundation.

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[3] Synthesized by Dr. John Biel, Lakeside Laboratories, Milwaukee.

tests indicated a definite improvement in mood and general outlook, and although the depression still existed, it seemed realistically based, and was considerably less overwhelming. The patient, however, refused to go back to his psychotic wife, and was returned to a state hospital.

*Case No. 2.* A 33 year old unmarried white man complained of depression, extreme apathy, and a chronic spastic colitis. He had quit his job over a year ago because of an increasing depression, accompanied by feelings of inadequacy and lack of desire to work. Psychological tests revealed him to be immature, with little or no affect, no signs of anxiety, and no insight into his condition. He reacted to 10 mg of JB–329 in much the same manner as the previous patient, covering a time-span of 18 hours. At the end of this period, he appeared very cheerful, and all of the depressed, haunted features of his face had disappeared. He gave the impression of a man well on the way to recovery after a long illness. That same day he indulged in a rather vigorous game of baseball, mixed, and talked freely with the other patients. He admitted feeling more aggressive and exuberant, and expressed a desire to go back to work as soon as he was discharged. Psychological re-examination showed him to be more responsive, less inhibited, and his outlook less limited. The patient was discharged two days after receiving the drug, and two days later he procured a position, which he still retains after three months.

*Case No. 3.* A 47 year old married man, had a history of intermittent depressions since 1953. He had been unable to work during the past year because of the depression. At the time of his admission he showed symptoms of restlessness and extreme agitation; he was harassed by self-accusations and feelings of guilt. Pre-therapy tests revealed an inadequate personality with an extremely passive dependence on other people. The existent anxiety and depressive features were overlaid upon a long-standing character disorder. The patient's response to 12 mg of JB–329 differed from the previous patients only insofar as the hallucinatory episodes were far more vivid and of longer duration. After 36 hours, the patient exhibited marked increase in motor activity and a dramatic improvement in mood. Psychological re-examination revealed that he was now able to express hopeful and resolute attitudes toward the future, although he still had little confidence in his ability to achieve the goals he envisioned. Two weeks after being discharged, he spontaneously wrote a letter from which were taken the following statements: "For your information, my progress has been good. I am working about full time . . . I have gained about ten pounds. My appetite is very good now . . . I am extremely grateful to you for what you have done."

*Case No. 4.* This patient was a 54 year old white married woman who appeared very much older and had been in a very severe depression for the last ten years. She had phobic paranoid reactions, suicidal ideas, and hysterical attacks accompanied by screaming, excessive crying, and other indications of desire for attention. Psychological examination indicated an unsound personality structure which seems to have been infantile even before the onset of the present illness. The effects produced by 12 mg of JB–329 were similar to those in the other patients, and lasted for 24 hours. The following day, she appeared more vivacious and most of the outward signs of her illness had disappeared. On the succeeding day, she socialized for the first time with other patients, and participated in occupational therapy activities. She seemed surprisingly cheerful, enjoyed her food, and appeared outgoing. After three days, when her husband came to take her home, she reacted violently and relapsed into her previous condition. Her condition was apparently developing into a full-blown psychosis. Electroshock therapy was administered during the next week, and although the pa-

tient showed improvement at first, she again relapsed into the previous agitated depressive condition.

*Case No. 5.* A 46 year old white unmarried female with paranoid delusions was depressed and apathetic. She was extremely tense and anxious, and her grasp on reality was tenuous. Her reaction to 10 mg of JB-329 was similar to that of the other patients, except that the hallucinations and disorientation lasted up to 36 hours. Two days later, she appeared definitely animated, cheerful, and composed. When questioned about her past condition, she replied, "I feel much more alert and don't feel depressed. Strangely enough, this was one of the first things I noticed. I feel now as if before the treatment I had been living in a flat two-demensional world and I had sort of retreated into myself, and now, after this treatment, I feel I am out in the normal three-dimensional world. I feel much more alive... I have more energy and enthusiasm." The patient resumed her work on the day following her discharge. She continued to show improvement during the next few weeks, although after one month she appears to be relapsing into her former state. She reported, however, that a symptom, which she referred to as a "catatonic nightmare," a condition during which she seemed to be conscious but was unable to move and which had existed for many years before the treatment, had completely disappeared and had not yet returned.

## DISCUSSION

Five cases have been briefly presented which serve as pilot experiments in the application of the piperidyl benzilates to patients manifesting psychopathology. Of the five cases, the first and the fourth can be considered as experimental successes but therapeutic failures. These two particular cases have never responded well to any other form of therapy, including electroshock and drugs.

In three cases (Nos. 2, 3, and 5) the single application of the experimental drug proved to be of therapeutic value. Cases No. 2 and 3, who were unable to work for over a year before the experiment, were able to do so. Case No. 5, which is the most interesting of our small experimental group, was working prior to the experiment; but the patient's statements and our objective observation are both indicative of the therapeutic effectiveness of the drug. The fourth case proved to be a therapeutic failure with respect to the drug, but the patient also failed to recover after electric convulsive treatments.

All five cases treated had only one symptom in common—some degree of depression. The other most remarkable common feature of cases No. 2, 3, 4, and 5 was an extreme infantile personality which could not be expected to change after a single treatment of whatever sort. If it were not for the fifth case, where the most remarkable changes were produced, this drug, JB-329 and its congeners could be earmarked for the treatment of depressive states only. In the fifth case, however, beneath the light depression were deeper disturbances of thinking and perception eluding superficial observation. In effect, she was psychotic. Whether her particular paranoid state should be diagnosed as latent schizophrenia, affective psychosis, or schizophreniform is beside the point. The importance of this case is that it indicates some usefulness of the piperidyl benzilates in a patient with marked perceptual and cognitive disturbances.

There are a great number of questions unanswered by this preliminary experiment. Both the extent and duration of improvement have not been fully assessed. It remains to be determined 1) whether repeated administration of the drug in hallucinogenic doses would have produced a greater degree of improvement in the successful cases and total or partial improvement in the unsuccessful fourth case; or 2) whether the production of the psychotogenic state is neces-

sary at all to produce improvement; or 3) if daily repeated small doses of the drug for an extended time would have produced the same but slower improvement. Both the effect and proper dosage schedule of a maintenance amount of JB-329 have yet to be determined. Finally, the proper field of application of this drug in psychiatry is in doubt. As far as the experimental results on normal and pathologic subjects permit any conclusion, the drug would be applicable to depressive states. Our fifth case, however, raises some slight hope that JB-329 or related derivatives might be useful in treating the grave personality disorders commonly diagnosed as schizophrenia.

The use of anticholinergic agents in the treatment of schizophrenia is not new. Forrer and co-workers (3) administered very large doses (up to 200 mg) of atropine intramuscularly to schizophrenics manifesting some degree of anxiety. Such doses of atropine produced coma, but most of the psychotogenic and stimulating actions achieved with JB-329 were absent. It remains to be seen whether the basic mechanism of these two modes of therapy is similar, although our findings suggest that atropine is devoid of the excessive stimulating properties of JB-329. LSD-25, another hallucinogen, has been used therapeutically in treating psychotics, largely as an adjunct to psychotherapy or electroshock convulsions (5, 7).

With regard to the mode of action hardly more can be said than that the substance has definite anticholinergic properties, but evidence that the central effect itself involved cholinergic blockade is lacking (1, 2). The piperidyl benzilates in smaller doses produce facilitation of motor neurons (Renshaw cells) in the lumbar region of the cat's spinal cord, while larger doses produced complete inhibition (8). Acetylcholine is presumed to be a mediator in Renshaw cells which are believed to exercise a generalized suppression in motor neurons innervating skeletal muscle. Himwich (4) has demonstrated an inhibition of electrical activity in the reticular bulbar formation of the rabbit with 2.5 mg/kg of JB-329, in contradistinction to LSD, which is excitatory. Such neurophysiological studies are merely preliminary, and although they may explain certain effects of the drug such as hypereflexia, considerably more work of this sort remains to be done.

The clinical results with the drug are even more obscure, particularly since the therapeutic effects become apparent long after the hallucinations and autonomic symptoms have disappeared. Furthermore, studies on animals indicate that the drug is readily hydrolyzed in the body, and is completely eliminated in 24–48 hours. One can only conclude, therefore, that therapeutic effects are related to the drug in a secondary manner. The piperidyl benzilates probably serve as a trigger mechanism for a long series of neurophysiological effects resulting in the improvement in the patient's psychopathological status. Subsequent clinical work is aimed at working out proper dosage schedules, as well as the indications for the use of this and other related drugs.

## SUMMARY

A new anticholinergic psychotomimetic agent, N-ethyl-3-piperidyl cyclopentylphenyl glycolate (JB-329), has been used in the treatment of a small number of depressed patients. The drug induces a drive of activity accompanied by some mood elevation. This seemingly desirable effect from a therapist's viewpoint occurs after a period in which there are psychopathological effects of a definitely psychotic nature. The post-psychotic effects which seem desirable are of a prolonged duration (days to weeks possibly). There is at least slight evidence in two cases of a continuing state of improved integration of the mental functioning and behavior.

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# THE USE OF DOXYLAMINE IN SCHIZOPHRENIA: PITFALLS IN THE EVALUATION OF A NEW DRUG[1]

MELVIN L. SELZER, M.D.[2] AND HERBERT WALDMAN, M.A.[2]

Doxylamine[3], an effective anti-histamine (Decapryn®), has been used clinically in the treatment of allergic diseases for the past several years. Drowsiness had been reported in sixteen to thirty-two percent of patients taking between 50 and 200 mgms of the drug daily (3, 5, 7). This phenomenon led Ferguson to suspect that the drug, in heavier doses, might influence the behavior of psychotic patients (6). Ferguson used the drug in doses up to 1600 mgms daily on 108 chronic female psychotics without any deleterious side effects; drowsiness was not a problem. He noted that daily doses in excess of 900 mgms did not produce any significantly better results.

The overall results of the above study were quite good, particularly in patients exhibiting periodically unpredictable behavior and in patients suffering from marked hallucinations and delusions. In addition, the drug was reported to be of value in patients who had improved moderately on other drugs but who were making no further progress.

Inasmuch as the drug appeared promising, a three month Doxylamine project was undertaken at the Ypsilanti State Hospital where a chronic schizophrenic population was available. Ypsilanti is essentially a service hospital and ward personnel are not particularly trained in nor comfortable with research methodology. This led to some difficulties and served to underline the subtle influences bearing on research involving human beings.

Three "back wards" on the male service were selected for the study. These wards have a preponderance of chronic psychotic patients, mostly schizophrenes, with a scattering of general paretics. Patients were selected who were in the hospital two or more years, and who were either periodically violent and destructive or markedly delusional and hallucinatory. The ward supervisors and assistant ward supervisors participated in the planning of the study and the selection of patients. Although they seemed to understand the stipulated selection criteria, at the same time they distinctly tended to prefer selecting subjects along two different lines. They favored the inclusion of patients in whom they had some positive emotional investment, and conversely also wished to include patients who were especially obstreperous and uncooperative on the ward. Their reasons were self evident.

Once this difficulty had been resolved, a double blind technique was outlined. The patients were divided into two comparable groups in terms of diagnosis, age, and length of hospitalization. One group received only placebo containing an inert powder that was indistinguishable from the Doxylamine capsules. With the exception of one pharmacist, no person at the hospital knew which patients were receiving drug and which placebo. The placebo aspect of the study caused some consternation among ward personnel. "Suppose," said one hitherto willing worker, "we say a patient is getting better, and then it turns out he isn't getting anything! We'll look mighty silly, won't we?" Despite ex-

[1] Read before the 114th Annual Meeting of the American Psychiatric Association, San Francisco, May, 1958.

[2] From the Ypsilanti State Hospital, Ypsilanti, Michigan. Dr. Selzer is now at the Department of Mental Hygiene, University Health Service, The University of Michigan, Ann Arbor.

[3] Doxylamine is the generic name for 2-[(a-(2-dimethylaminoethoxy)-a-menthylbenzyl)]-pyridine. The drug and placebo were supplied through the courtesy of the Department of Medical Research, The Wm. S. Merrell Co., Cincinnati.

planations and reassurance, this man remained somewhat defensive about rating patients through the early weeks of the study.

Initially, every subject patient in each group received one 100 mgm capsule of Doxylamine (or its placebo counterpart) three times daily (t.i.d.). Once a week the ward supervisor and assistant supervisor would rate the patient using the Gardner Behavior Chart (8). In addition they would record a spontaneous overall impression of the patient's condition (*i.e.* a written evaluation as contrasted to the numerical Gardner Chart Rating). In these assessments they were encouraged to use nontechnical language. Every two weeks the ward physician would join in rating the patient. At these times, if little or no improvement had occurred during the preceding two weeks, the patient's dosage was raised by one multiple. Hence at the end of two weeks unimproved patients were getting 200 mgms t.i.d., and after four weeks they were receiving 3 capsules t.i.d.—the maximum dosage.

After three months, each patient received a final rating on the Gardner Chart and a final written summary of any change in his condition over the three months interval.

## DESCRIPTION OF GROUPS

The placebo and Doxylamine groups each consisted of 19 patients; 17 schizophrenes and two general paretics. The latter were included as an additional control.

The placebo group's mean age was 47.5 years with a standard deviation of 11.8 and a range from 23 to 67 years. The Doxylamine group had a mean age of 42.2 with a standard deviation of 11.0 years and a range of 21 to 65.

The mean duration of hospitalization was 12.2 years (standard deviation 7.2) for the placebo group and 10.6 years (standard deviation 7.6) for the drug group. The ranges were two to twenty-five and two to twenty-four years respectively.

## RESULTS

Inasmuch as there was a high correspondence between the spontaneous written evaluations on each patient and the Gardner Ratings, there is no need to discuss the Gardner Chart Ratings in detail. The Gardner ratings were analyzed by an analysis of variance technique. This showed no differential in the amount of improvement between the two groups. No one criteria from the Gardner stood out significantly; where improvement was noted, it was uniform. The drug did not appear to exhibit any marked antihallucinatory or antidelusional effect.

Upon completion of the study, both the weekly and final evaluations and ratings were used to grade the degree of improvement attained by the patient according to the improvement classification used by Barsa and Kline (1).

Of the 19 placebo patients, 11 were unimproved, five slightly improved, two moderately improved, and one markedly improved. Eliminating the two general paretics (both unimproved), nine patients out of 17 were unimproved.

The Doxylamine group had 13 unimproved, two slightly improved, three moderately improved and one markedly improved. Again omitting the general paretics, (one unimproved and one slightly improved) 12 patients out of 17 were rated as unimproved.

The most remarkable single change was that of a 50 year old catatonic schizophrene who had been a patient at the hospital for 21 years. During those years he remained withdrawn and motionless except for frequent bizarre, agitated outbursts when he would destroy his clothing. He required constant supervision, soiled and wet himself, and never spoke to anyone. He was often observed moving his lips as if in response to auditory hallucinations.

After the third week, this patient began conversing with the astonished "back day room" attendant; this for the first time in over 15 years. At four weeks he had stopped

tearing his clothing, was keeping himself neat and clean and had been promoted to a day room that required very little supervision. This improvement continued throughout the three month period with the patient participating in more and more off-ward hospital activities.

When the capsules were discontinued he slowly regressed to his previous state. It was later noted that he had in fact been on placebo.

### POSSIBLE SOURCES OF ERROR

One vulnerable aspect of this and other tranquilizer studies is the emotional involvement of persons doing the evaluative work. If personnel are desirous of seeing appealing or obnoxious patients get well, there is a tendency to give these patients unduly optimistic ratings, at least initially.

A second possible source of error lay in the fact that raters were always able to see the ratings of previous weeks. Methodologically more desirable would be to remove each week's written comments and numerical ratings when they were completed.

The experiences of this project suggest that it might be best not to inform ward personnel that a placebo will be used.

### SIDE EFFECTS

Blood pressures were taken weekly for the first month and every two weeks during the ensuing two months. One patient on Doxylamine had a marked hypotensive reaction. His blood pressure had been 130/80 and it dropped to 100/70 over a two week interval. Consequently his dosage was left at 100 mgms t.i.d. but one week later he went into shock with sudden syncope, pallor, and a B.P. of 82/64. He was given adrenalin 0.5 cc, caffeine and sodium benzoate, and placed in Trendelenberg. Two hours later his blood pressure rose to 88/64 and had reached 110/80 by the following day.

Two patients complained so bitterly and persistently of somnolence and fatigue that their dosage had to be reduced. Later, both were found to be on placebo. Toxic reactions to placebo are neither surprising nor unknown. Inasmuch as profound tissue responses may occur following placebo administration, toxic reactions may represent pathological variants of these responses (9). Toxic reactions ranging from mild to extremely severe have been reported in other placebo studies (4). It is not far-fetched to postulate that these reactions are a function of the relationship between the patient and the person whom the patient perceives as having given him the medication.

### DISCUSSION

In this small group of chronic psychotic patients, Doxylamine did not appear to yield notably positive results. However, the patients received little or no environmental or emotional support with the capsules. Another mitigating consideration was the fact that the study dealt with a very chronic and poor prognostic group.

Turning to the placebo group, it appears that these patients showed as much improvement as did the drug group. (In the Gardner Ratings the groups were indistinguishable.) This is less than surprising if one recalls the importance of suggestion and the psychological impact of *any* medication. Beecher summarized 15 placebo studies in which placebo was given to post-operative patients to relieve pain and discomfort (2). The average significant effectiveness of the placebos was 35 $\pm$ 2.2 percent. In dealing with patients whose illness is at least partly, if not entirely psychological, the placebo effect can be expected to be at least as significant. Beecher points out that "unawareness of placebo effect can be devastating to experimental studies as well as to sound clinical judgement." Nevertheless most studies done with tranquilizers—in fact the overwhelming majority—have been conducted without any controls and all patient improvement has then been attributed to

the drug. In lieu of adequate controls, these studies often rely on creating an impression of reliability by using large numbers of patients. This is hardly justifiable, since the placebo effect may occur in any event.

Many drugs have been endorsed in the past on the basis of poorly controlled studies, and when the sole effect was that of a placebo. It is time that our knowledge of placebo effect was put to use in double blind studies of the tranquilizers. Only thus will any real pharmacological advance be made. Scientific considerations demand that the valid evidence on the power of placebo be utilized in tranquilizer studies.

SUMMARY

Doxylamine, used previously as an antihistamine, was given to a small number of chronic psychotic patients at a state hospital. The experimental study was of three months duration and doses up to 900 mgms per day were administered. A double blind technique was used, one-half the patients receiving a placebo. Seventy percent of the Doxylamine patients and fifty-three percent of the placebo patients remained unimproved. Side effects were virtually non-existent; one patient on the drug had an acute hypotensive reaction.

A plea is made for the adoption of double blind placebo techniques in the evaluation of drugs used in treating the mentally ill.

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BRIEF COMMUNICATION

# ANALYSIS OF THE PERSONALITY STRUCTURE OF 26 ACTUAL SUICIDES

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Until quite recently there has been a dearth of literature on the personality structure of psychiatric patients who commit suicide. Farberow (1) used the Minnesota Multiphasic Personality Inventory to study patients in a California veterans psychiatric hospital and found that patients who made suicide threats differed significantly in their test profiles from patients who made suicide attempts. He also noted that the profiles of the threat group indicated a much greater severity of disturbance than did those of the attempt group. The profiles of the attempt group, however, were not significantly different from those of a control group of psychiatric patients-in-general.

Rosen, Hales and Simon (2) replicated this study and obtained similar results. They concluded that in any investigation of suicide more meaningful results might be obtained if individuals with various kinds of "suicidal" behavior are differentially classified.

Finn (3) studied 20 consecutive admissions to an army hospital for suicide attempts and gestures and found such traits as impulsiveness and depression to be significant, but concluded that suicide must be considered basically a result of a major defect in psychosexual development. He specified such defects as narcissism and poor masculine identification as important variables in the personality of many of his patients.

The present study is an analysis of the MMPI profiles of 26 psychiatric patients who subsequently committed suicide. Some of them had more than one admission to the Minneapolis VA Hospital and others were tested with the MMPI more than once during an admission. For this study, that profile was selected which was most recent to the time of admission and which was obtained during the hospitalization most closely antedating the suicide.

The mean age of the suicide group was 36.7 years with a range of 20 to 67, and a median of 37. Only one patient was in his sixties and three were in their fifties. Education varied from sixth grade to the medical degree, two patients being physicians and one a Ph.D. Median education was 12 years. Eight patients were single, 14 were married, three were divorced and one widowed. Marital status was not significantly different from a random group of patients from the same population. IQ ranged from below average in two cases to superior in 13 cases. This also was similar to the random group of patients from this population. Occupations varied and were consistent with the range of intelligence.

## ANALYSIS OF PROFILES

Comparison of the mean profile of the group of 26 actual suicides with the mean profile of each of the three groups previously studied—Thought, Attempt and Control—shows close similarity to the Control group. However, there is one difference between these two: the mean Masculinity-Femininity (Mf) score of the actual suicides is higher than that of the control group, at the 10 per cent level of significance (Figure 1). Like the control and attempt groups, the mean profile of the actual suicide group is significantly lower than

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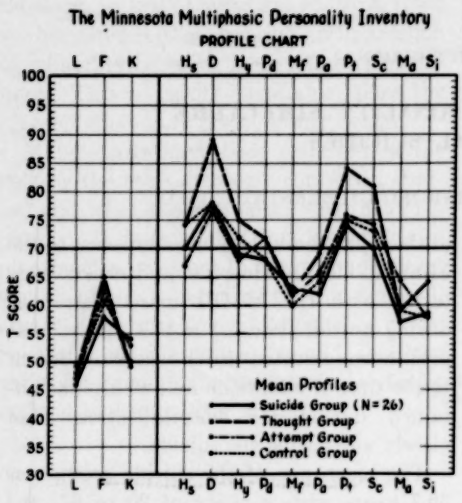


FIG. 1. Mean profiles of four groups discussed in text.

the thought group on the F, D, Pa, Pt, Sc and Si scales. The Ma score of the attempt group is significantly higher than that of the actual suicide group, suggesting, in conjunction with a previous finding of a significantly higher Pd mean score for attempts as compared to patients-in-general, that the most immature and impulsive individuals may be found more frequently in a suicide attempt group than in a group of actual suicides. Since Finn was studying patients who had made attempts and gestures, it is probable that impulsivity as a predominant trait would be found more often in his group than in a group of actual suicides.

Item analysis of the MMPI responses of the actual suicide group versus the control group, in an attempt to derive a scale to predict suicide, yielded 23 items which were statistically significant. However, this number of significant differences could be obtained by chance when running 550 significance tests at the 5 per cent level. A lack of meaningfulness of the set of items obtained indicates that such was the case. Cross validation also bears this out. These results suggest that it is not possible to construct a suicide scale for the MMPI which will have predictive value.

## COMPARISON OF PROFILE TYPES

The profiles of the actual suicide group were separated by inspection into several types which are familiar in daily clinical practice with this test. Nineteen of the 26 were considered as depressive types of curves. These can be divided into several clinical subtypes: 1. Anxious, depressed, ruminative, schizoid, severe neurotic (similar to the previously described "Thought" group); 2. psychotic depression type; 3. depression combined with immature character traits (impulsivity, irritability, narcissism); and 4. miscellaneous.

Seven of the 26 profiles are characterized by a lack of elevation on the D scale. They can be separated into three types: 1. pathological defensiveness as a primary trait; 2. marked denial and repression, but with considerable emotional lability, irritability and restlessness; and 3. extreme passivity.

There was no apparent relationship between personality type and choice of method. Only eight of the 19 cases with depressive profiles received a primary diagnosis of depression. Others were variously diagnosed.

## DISCUSSION

The elevation on the Mf scale in the mean profile of the suicide group could be interpreted as supporting the notion advanced by Finn (3), on the basis of his clinical study of 20 soldiers, that a defect in psychosexual development with resulting narcissism and poor masculine identification are important variables also in the personalities of actual suicides. To what degree and to what extent this might hold true within such a group, remains to be studied. The widely prevailing opinion that depression is a significant variable is borne out by our finding that 19 of the 26 actual suicide patients have profiles of a depressive type.

How these postulated traits manifest themselves in terms of behavioral response to environmental stress may be somewhat clarified by the frequent finding of previous attempts. In our group at least one-third of the patients had a history of one or more previous attempts, and thorough search into histories would probably increase this number. Shneidman and Farberow (4) have also noted the frequency of previous attempts in actual suicides. This, in conjunction with the fact that suicide occurred in several cases many years after one or more hospitalizations, suggests that, to use Lewinian terms, the suicides may tend "to leave the field" after a long succession of unsuccessful attempts to deal with what, for them, is perceived as an insoluble problem. For example, a deep need for the support of a marital relationship, but with inability, because of psychosexual immaturity, to succeed in such a relationship, may result in recurrent depressive episodes, frequent resort to alcohol, drugs, job changes, etc., and finally suicide.

However, the most salient finding of this investigation would seem to be the heterogeneity of personality types who commit suicide. Even the distinction made previously between a suicide thought group and a suicide attempt group, although significant for that sample of group data, does not hold up for the individual patients of the actual suicide group, since six of them had profiles which are very similar to the mean profile of the thought group. Suicide, like alcoholism, should therefore be considered a symptom which, although often associated with depression, cuts across personality and diagnostic types. Attempts to predict suicides are probably doomed to failure, because of the obvious difficulty in predicting the choice of symptoms for any individual. With a combination of severe depression, poor masculine identification, and a history of previous attempts, the chances might be increased for a suicidal outcome in our VA psychiatric population, but the base rate of suicide is so low, roughly five per thousand, that it would be betting against prohibitive odds to make such a prediction in any individual case. The suicide rate for patients with a primary diagnosis of depressive reaction would be much higher, somewhere in the neighborhood of two per cent, but still too rare to predict for the individual case, especially if the consequences of such a prediction would result in a decision for continued hospitalization. With a known predisposition to develop the symptom on the basis of a previous attempt, the rate would be still higher, but it is beyond the scope of this study to estimate this probability.


## SUMMARY

MMPI profiles of 26 psychiatric patients who suicided were analyzed.

Comparison of mean profiles with a suicide thought, attempt and control group revealed a higher Mf score for the suicide group.

Nineteen of the 26 patients had depressive profiles, whereas seven profiles were characterized by defensiveness and a lack of elevation.

Depressive and non-depressive profiles can be separated into a number of subtypes, which are described.

Suicide, like alcoholism, should be considered a symptom which, although often associated with depression, cuts across personality and diagnostic types.


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## BOOK REVIEWS

HAUGEN, G., DIXON, H. AND DICKEL, H. *A Therapy for Anxiety Tension Reactions.* Macmillan Company, New York, 1958. 110 pp. $3.50.

Very few psychiatrists make any use of Jacobson's relaxation methods, and this is not entirely justified by the shortcomings in the Jacobson system. Skeletal muscle tension can be a bad habit and such tensions have central effects that are more profound than a simple stiff neck or tension headache. This readable little book will make relaxation techniques more acceptable to a wider audience. Practical therapeutic procedures are clearly detailed while their theoretical formulations suggest a number of interesting research problems.

Although this book is readable, useful, and stimulating, it has a serious weakness. Since the psychiatric community has chosen to ignore Jacobsen, it would seem that Jacobson's disciples now feel they should ignore the contributions made by the rest of the psychiatric community. For example, the possibility of using relaxation techniques in combination with other psychotherapeutic procedures is largely ignored. Archaic and distorted interpersonal relationships are more pronounced under conditions of stress. At the same time, a large number of the tense, anxious patients seen in modern psychiatric practice are also troubled by character disorders; and stress or no, they habitually use infantile techniques to cope with adult problems. Whether tense or not, these people are ineffective human beings and no amount of musculo-skeletal retraining will correct the situation. Such people need all the help modern psychiatry can offer—and more. It is unfortunate that advocates of certain therapeutic techniques have ignored what Jacobson might have to offer. By the same token, it is unfortunate that these advocates of Jacobson's methods have adopted an equally narrow viewpoint.

Enoch Calloway, III

HOLLINGSHEAD, A. B. AND REDLICH, F. C. *Social Class and Mental Illness.* Wiley & Sons Inc., New York, 1958. 442 pp. $7.50.

It may be of passing relevance to note that while engaged in collecting data for the study reported in this volume, some of the members of the research team felt the need to publish their reflections about the problems and strategies of interdisciplinary research. In a sense the book stands as an admissible reflection of these earlier observations. Whether there are real differences between the professions of sociology and psychiatry with respect to the communicative eloquence of its members, is moot, although the stereotype would certainly favor the sociologist. Surely there are important differences in conceptual approach, methodology and research technique. In a trial marriage of the two disciplines one would hope for a reasonable balance of investigative approaches notably different, and in this case vainly. Here the sociologist is clearly the dominant partner.

Written by a Professor of Sociology and the Chairman of the Department of Psychiatry at Yale University, this book reports a community study dealing in a variety of ways with the relation of social class to mental illness. A companion volume by two other members of the research group will complete the report. A large team of investigators collected material for the study over a period of some four years. Psychiatric patients residing in the metropolitan New Haven area and under treatment during a given six month period, were used as the experimental sample. Psychiatric and sociological data were obtained for each

case, and painstaking care was taken to ensure that all such patients were included. Thus the experimental group comprised not a random or representative sample, but a total population. To determine the social stratification patterns of the community as a whole, a much larger general sample of the New Haven area was used. This latter operation, yielding the control data that provide the key comparisons in the study, was apparently completed by the sociologist and his associates.

This is a carefully written, unpretentious, scrupulously honest and somewhat ponderous account of an investigation fraught with methodological difficulties. The authors are at pains to rehearse these problems and to clarify deficiencies in the context of their findings and their interpretations of them; on that account the value of the work as a scientific document is enormously increased. The reader may be seduced into making untoward generalizations from this study, applying what has been learned about this community to others. To a limited extent this may be done, but it should be stressed that there are a number of important qualifications to be borne in mind.

One must keep in mind, for example, that the psychiatric population here examined consists of patients under the care of qualified practitioners. This, then, is not a study of psychiatric illness at large. One must remember that, while the stratification scheme devised by Hollingshead to determine the class structure of the New Haven population could certainly be applied elsewhere, it would be unlikely that an equivalent patterning would result. In general terms, surely the same basic structure, but no two communities would be expected to demonstrate precisely the same social organization. As a matter of fact New Haven is ethnically unique among cities of its size. One must understand as well that this is by no means a typical community in terms of some of the variables being explored. The influence of the medical school and the training function of its Department of Psychiatry is reflected in markedly larger numbers of psychiatrists, and particularly psychoanalytically oriented psychiatrists, than are found in other population centers of this size. These and similar considerations are important, for they clearly relate to the numbers and kinds of patients that are treated.

As the findings are presented and discussed, the social status position of the individual unfolds as a powerful correlate of the kind of psychiatric illness he may develop if he becomes mentally ill, and the type of treatment he may receive. To an appreciable degree social class determines diagnosis, treatment, and is related to the prevalence of treated mental illness. The class-focussed hypotheses that have been tested in this investigation are not especially startling as general propositions, and the astute observer would successfully predict the general nature of the results. Yet it is to be appreciated that these relationships have been so conscientiously explored.

This is an arresting and significant documentary of present-day psychiatric practice, with important implications for remedying socially determined shortcomings. It requires and deserves a careful reading. It will be scrutinized and appreciated by many social scientists and their students. There is every likelihood that it will be less well received by psychiatrists. Looking with suspicion on the methodology, they will tend to deny altogether the usefulness of the findings, and more's the pity.

J. P. Le Boon

FARNSWORTH, P. R., Ed. *Annual Review of Psychology, Vol. 8.* Annual Reviews, Inc., Palo Alto, 1957. 512 pp. $7.00.

This book maintains the high standards of earlier volumes in this series, and its usefulness can hardly be overestimated. De-

voted to critical reviews of contemporary psychological literature in eighteen subareas; written by carefully selected, competent, and often outstanding representatives of their fields, who necessarily devote much time to the preparation of the respective chapters; the volume stands as a readable and ready reference for any one wishing to keep pace with current psychological theory and research. Here are available compressed and integrated overviews of published work of the previous year, the distilled yield of comprehensive searches of the literature. As a time-saver the book is of incalculable value.

Each of the writers, of course, is free to focus on those publications that he considers most noteworthy, and as a result there is some variation in completeness of coverage. A generally high level of objectivity is maintained, however. The reviews are especially effective in that they amount to more than a series of organized abstracts; an evaluative, interpretative approach is used. In the present volume the reviews by E. Stellar on physiological psychology, by E. L. Walker on learning, and by C. L. Winder on psychotherapy, among others, impress as outstanding.

H. A. Robinson

WARTENBERG, R. *Neuritis, Sensory Neuritis, Neuralgia:* A clinical study with review of the literature. Oxford University Press, New York, 1958. 444 pp. $8.50.

This book is precisely what its title denotes, since it primarily presents an extensive review of the literature dealing with the clinical aspects of neuritis. Throughout the volume the author has stressed his personal views concerning the common role of inflammation in most of the affections of the peripheral nerves which are discussed. The author additionally presents case histories of migrant sensory neuritis which he relates to multiple sclerosis.

The value of this volume lies chiefly in the extensive review of the literature, past and recent, and the extensive bibliographies compiled. Each chapter has its own special bibliography and, in addition, there is presented a general list of references at the conclusion of the book. There is also a serviceable index.

Any criticism which might be made of this work would be regarding the unusual stress the author has placed on the role of inflammation in neuritis of all types without apparent good evidence.

This book is of value and interest to all who deal with the clinical aspects of the nervous system.

Charles Van Buskirk

WOODHALL, B. AND BEEBE, G., Eds. *Peripheral Nerve Regeneration.* Veterans Administration Medical Monograph. U. S. Government Printing Office, Washington, 1957. xxiv + 671 pp., illus.

This is a report of a study on peripheral nerve injuries commenced in 1943 by members of the Armed Forces and others. Representatives of the Veterans Administration and the National Research Council also participated. This volume contains a wealth of information which could not be obtained in civilian practice but which should be of great value to the civilian physician. The data is treated statistically as far as this is possible. All methods of dealing with various types of nerve injuries are described and compared. A number of the common complications such as infection, associated vascular injury, associated bone fractures and causalgia are considered in relation to peripheral nerve regeneration. Motor, sensory and autonomic recovery are considered separately and in addition the total functional recovery of the individual is evaluated. An attempt is made to evaluate the regeneration potential of individual nerves and methods of determining prognosis are also discussed.

A short bibliography is included at the

end of the volume, as is also an index of subject material. The latter is not as helpful as it might be. This book will be most useful as a reference volume by practitioners of clinical neurology, neurosurgery, and physical medicine.

Charles Van Buskirk

FISHER, S. AND CLEVELAND, S. *Body Image and Personality*. D. Van Nostrand Co., Princeton, 1958. xi + 420 pp. $9.25.

Although much has been written on the subject of body image, the publishers do not err in referring to this work as a "pioneering study". The problem area is an old one but the approach in this instance is both novel and promising. By many standards this book is an impressive work. Not its least impressive aspect is a scholarly and readable summary of the literature pertaining to body image found in Chapter One. Fisher and Cleveland first present an extensive survey of the neurological, psychiatric, and other literature pertaining to this topic and discuss the relevant theoretical formulations by general psychology, Freudian and other psychoanalytic schools. This historical survey will undoubtedly become required reading for anyone interested in this sometimes baffling but always intriguing area of clinical study and research.

This survey is followed by the presentation of a fresh approach to the study of body image, both in the specificity of its focus and in the care the authors have taken to construct a reliable and objective measuring instrument. Rather than concern themselves with body image as a vague generality, Fisher and Cleveland have set out to study the boundary dimension, because they assume that "a boundary measure has unusually strategic import in predicting the behavior of an organism in the medium that surrounds it" (p. 345). After preliminary studies in which material relevant to the boundary dimension was sought in interviews as well as in the Rorschach, TAT, and Draw-A-Person tests, the authors agreed on the Rorschach as the richest source of information. Two Rorschach content scales resulted. The Barrier Scale (hereafter BS) is assumed to provide an index of the firmness and definiteness of the boundary of the body image, the Penetration of Boundary Scale (hereafter PBS) an index of the weakness, and penetrability of the body image boundary. Several interscorer reliability coefficients ranging from .82 to .99 based on the rank ordering of total scores are cited. Because their early studies demonstrated that the PBS scores differentiated only between certain abnormal groups, and failed to differentiate between various groups of normals, the BS score was retained as the sole predictive measure in most of the subsequent studies.

As one glances through the volume one experiences both amazement and incredulity that such a wide range of behavior phenomena could be successfully predicted from a single measure. This is a frail vessel indeed for the heavy cargo it carries and for the widely ranging course the authors have charted for it. That this incredulity may not appear as a sour sort of skepticism, the reviewer feels obliged to summarize briefly the major findings of the studies reported in the book.

The authors themselves are quite exhilarated by the wide scope of their findings and exclaim in their concluding chapter "The Body-Image boundary dimension has shown itself to have a powerful potential for predicting a wide range of behaviors. It has permitted prediction of such diverse phenomena as psychological adjustment to poliomyelitis, modes of interaction of small groups, and patterns of psychological reactivity" (p. 345). Much of the rest of the book is a presentation of the detailed findings that occur within the broad boundaries so sweepingly drawn. Some of these detailed findings pertain to psychosomatic correlates of the boundary dimension. Thus, subjects with such exterior body ailments as arthritis

and neurodermatitis are found to possess firmer body image boundaries than subjects with such interior body symptoms as stomach disturbance and colitis. With normal subjects (undergraduate college students) high barrier scores are positively correlated with the number of exterior symptoms reported, primarily involving the skin and musculature. The studies that appear most exciting to the authors are those dealing with physiological reactivity in relation to the boundary schema. They report data to support their hypothesis that "persons with definite body image boundaries would manifest a reactivity pattern such that responses involving the outer body layers would be relatively high and those of the body interior low; whereas persons with undifferentiated body boundaries would exhibit a pattern in which body interior response is high and body exterior response low" (p. 311). This hypothesis is supported by such results as a positive rank order correlation between barrier score and light touch sensitivity and by a tendency for high barrier persons under surgery to manifest lower minimal heart rates than low barrier persons. By contrast, under conditions of stress the low barrier person responds with an increase in heart activity while the high barrier person responds with an increase in peripheral resistance.

Several categories of research deal with behavior that is more grossly observable. Many of these studies depict the high barrier person as essentially a self-steering individual. Thus, he is likely to be less suggestible than his low barrier counterpart. He sets higher goals for himself and pursues them with more drive. He has a superior ability to adapt to a variety of stress situations and is more likely to adopt an active course in dealing with environmental frustrations. This tendency toward an extroverted outlook is borne out by another series of value studies. These lead the authors to conclude that occupational groups and interest patterns that stress communication with and about people are associated with significantly higher BS's than those that stress things and abstract concepts. Thus psychologists, anthropologists and artists have significantly higher barrier scores than physicists, mathematicians and chemists. This surprising consistency in results also extends into the area of group behavior. High barrier groups demonstrate a higher level of participation by all group members, and a more democratic process of operation, than do low barrier groups in which individual initiative is low and dependence on authoritarian lead, high.

In fact, there is hardly an area of personality study that has been neglected. The authors have something to say about such additional matters as the relationship between their barrier score and family patterns, sex, culture, the site of cancer, neurosis and psychosis.

How can one assess this staggering accumulation of varied data? Are we indeed face to face with an impressive historical discovery in the difficult study of personality development? Or is this volume a somewhat pretentious, inflated presentation of some data perhaps interesting and significant in a modest way, but lacking the generality imparted to it by the authors? Is the barrier score a measure of a basic etiological determinant of personality growth, or simply a correlate of certain phenomena?

This task of evaluation is made difficult by the vigor with which Fisher and Cleveland have pursued their research. A rough count shows that they have either carried out themselves or directed approximately 60 studies in which 340 predictions were made. The statistical technique used was almost invariably the Chi Square test of significance of differences between groups. The 340 predictions made were sustained by about 215 differences in the anticipated direction, of which roughly 180 were sig-

nificant. This is a most convincing box score.

There is, however, some evidence of overexuberance on the part of the authors. While they frequently remind the reader that their studies are exploratory, they do not always speak as though they themselves actually believe this. Dispersed throughout the book one can find premature generalizations and over-excited theoretical pronouncements. The following conclusion is a case in point. "The findings support the general proposition that psychological factors do play a part in phases of the cancer process. They also support the specific proposition that the character of an individual's body image boundaries may influence the body site at which he develops cancer" (p. 306). This conclusion is based on a study in which an *exterior* group consists of one man with skin cancer, six women with melanomas and 52 women with breast cancer, and an *interior* group of one woman and two men with cancer of the colon, two men with cancer of the lung, one man with cancer of the stomach and 24 women with cancer of the cervix. A higher barrier score was obtained for the exterior than for the interior group. This interesting but highly tentative finding is hardly an adequate basis for the definitive conclusion quoted above.

Moreover, methodological questions might be raised about the propriety of combining heterogeneous subjects into single sub-groups, a practice that the authors follow with disturbing frequency. One might be inclined to take a lenient view of such imperfections in design in rough exploratory studies. Indeed, an insistence on greater rigor would have made it impossible for the authors to exercise the agility that they show in seeking out natural experimental situations and in strategically exploiting data originally collected for other purposes. The free-wheeling mobility with which they have pursued their research is one of the stimulating features of their work. Yet it must be apparent that the time has come for replication and the more rigorous testing out of their promising leads.

In summary, Fisher and Cleveland have written a most scholarly and readable book on a subject that has been obfuscated in the past. They have isolated what they consider to be a single crucial aspect of body image, the boundary dimension, and have developed a reasonably objective and reliable instrument for its measurement. With a persistent singleness of purpose over a number of years they have collected data regarding many psychological, neurological, sociological, and physiological correlates of their barrier scores with an amazing consistency in results. The major criticism is their frequent failure to emphasize the exploratory nature of their work in their conclusions and theoretical formulations, with a resulting tendency to speak as though they have indeed made a major discovery regarding a basic determinant of personality development.

What can one reasonably say about the boundary dimension on the basis of the present book? There is no convincing evidence of a central causal role for the body image boundary in behavior. The data do, however, support the assertion that the body image boundary is a more accurate reflection of central personality attitudes than of actual body structure. Such an assertion is consistent with the clinical hunch that body image could be used as a diagnostic index of personality structure, if one were able to evaluate it reliably. In the same vein the following conclusion appears plausible. "We have assumed that it is this position of the body, intermediate between 'outside' and 'inside' which makes it a unique projection screen for patterns of attitudes; and we have concluded that the body image is formed of these projected attitudes" (p. 387).

This quality of body image has, of course, long intrigued clinical psychologists with its potential as a projective device in personality study. The reliable and valid evaluation of body image has, however, continued to elude us. Fisher and Cleveland appear to have devised an effective measure of one aspect of body image, a significant contribution in itself.

Benjamin Pope

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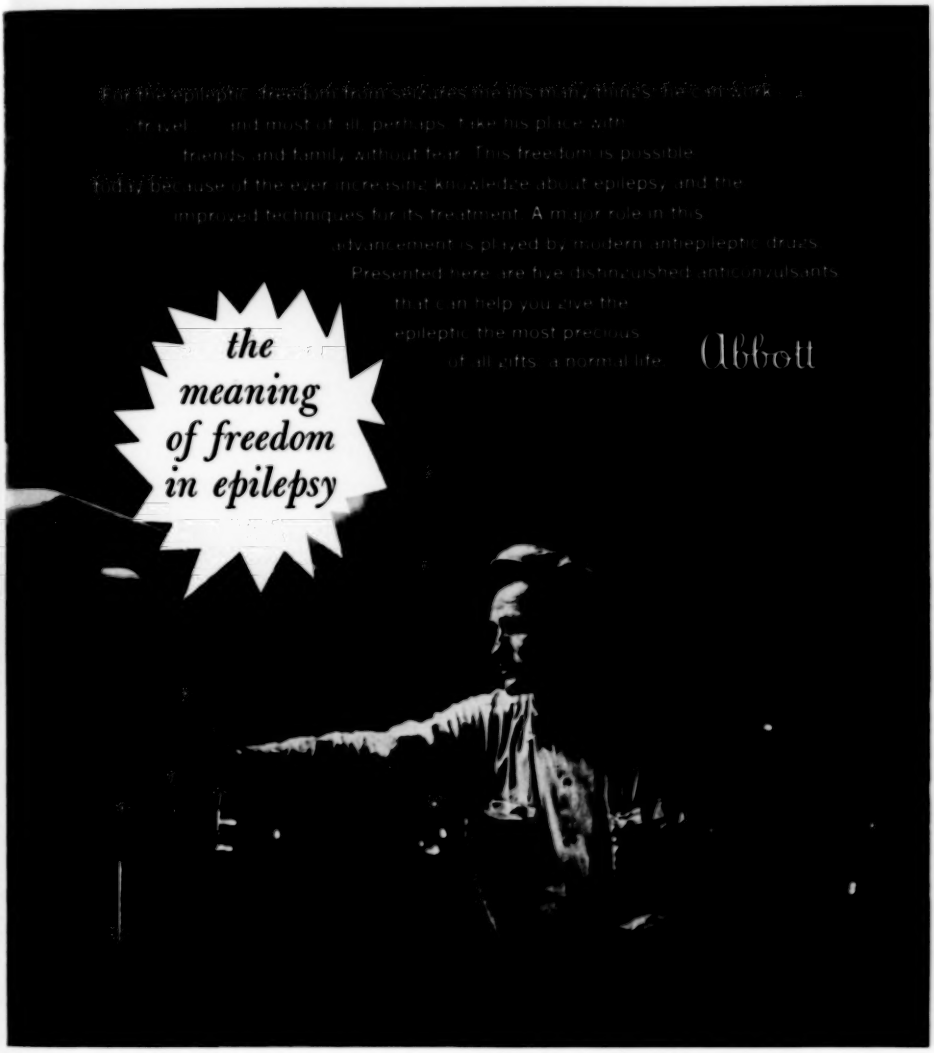


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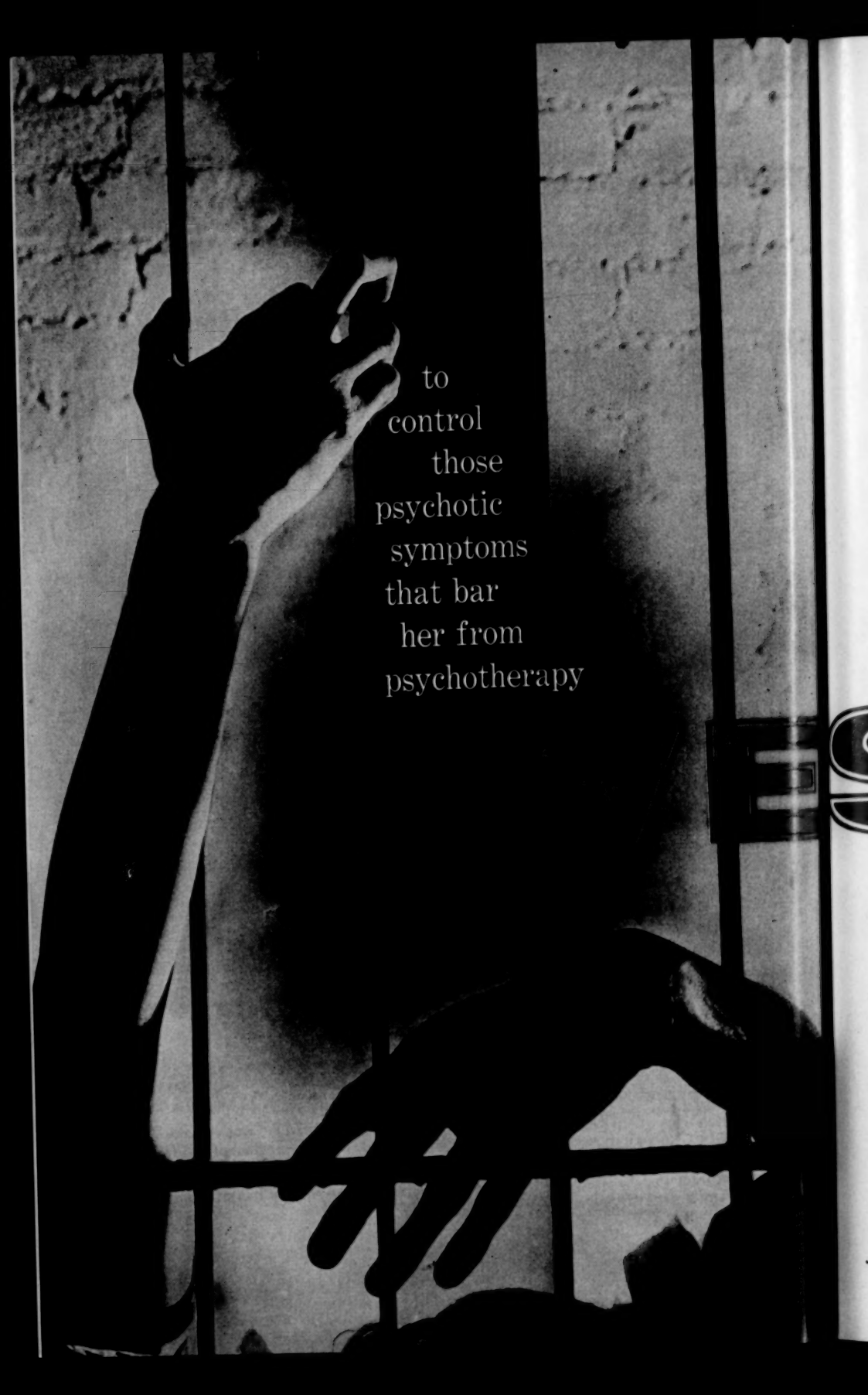
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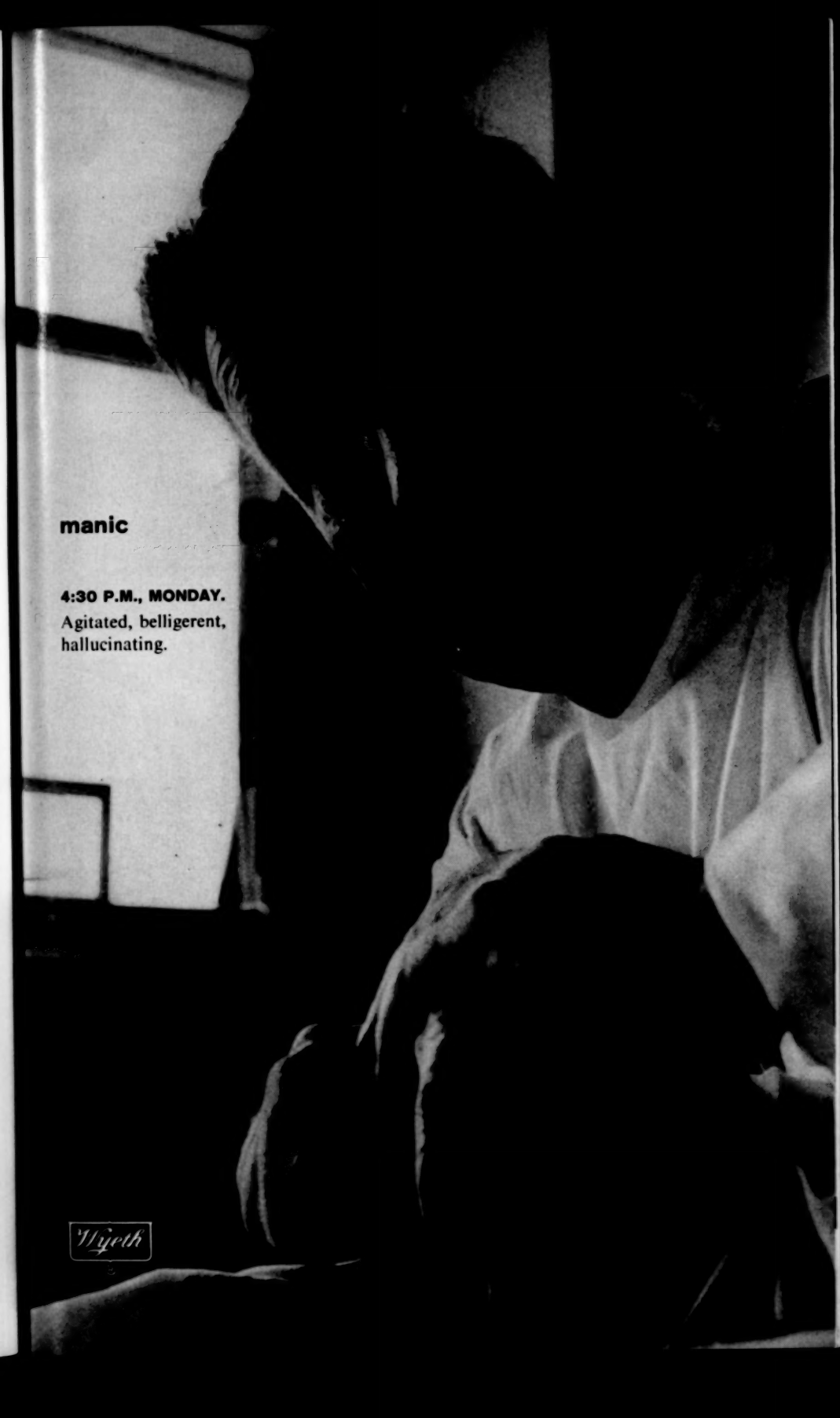
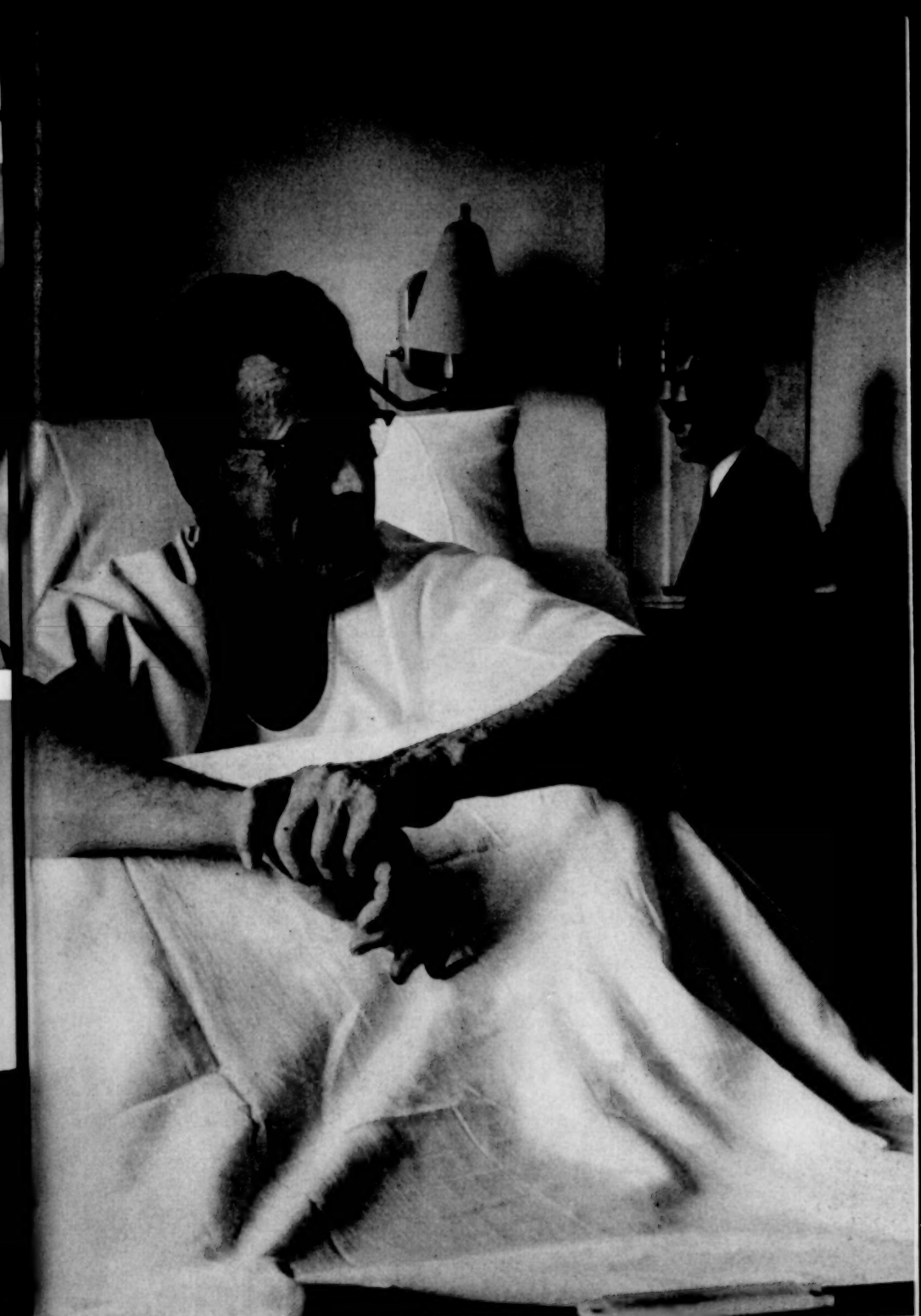

manic
4:30 P.M., MONDAY.
Agitated, belligerent, hallucinating.
Wyeth

**4:40 P.M., MONDAY.** SPARINE I.V.

**5:00 P.M., MONDAY.** Calmer, less hostile. Respon
cooperatively to questions.

**7:30 A.M., TUESDAY.** Refreshed but some agitation remains. SPARINE I.V.

1:10 A.



**1:10 A.M., TUESDAY.** Relaxed, nonhallucinating, alert. SPARINE orally for maintenance.

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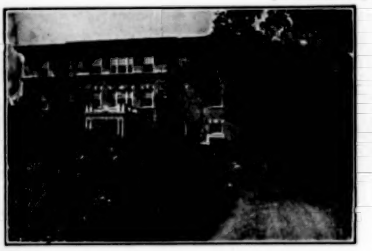

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